```
     (FILE 'HOME' ENTERED AT 12:41:27 ON 13 SEP 2000)

     FILE 'REGISTRY' ENTERED AT 12:42:20 ON 13 SEP 2000
L1             STRUCTURE UPLOADED
L2               4 S L1 SSS SAM
L3             100 S L1 SSS FULL

     FILE 'STNGUIDE' ENTERED AT 12:50:55 ON 13 SEP 2000

     FILE 'REGISTRY' ENTERED AT 12:55:16 ON 13 SEP 2000

     FILE 'MARPAT' ENTERED AT 12:56:56 ON 13 SEP 2000

     FILE 'REGISTRY' ENTERED AT 12:57:39 ON 13 SEP 2000

     FILE 'MARPAT' ENTERED AT 12:58:20 ON 13 SEP 2000

     FILE 'CAPLUS' ENTERED AT 13:00:06 ON 13 SEP 2000
L4             186 S L3
L5               0 S 2' DEOXY 2' FLUORO RIBONUCLEOSIDE AND L4
L6               0 S 2'(W)DEOXY(W)2'(W)FLUORO(2W)NUCLEOSIDE

     FILE 'REGISTRY' ENTERED AT 13:06:52 ON 13 SEP 2000

     FILE 'HCAPLUS' ENTERED AT 13:08:09 ON 13 SEP 2000

     FILE 'REGISTRY' ENTERED AT 13:08:44 ON 13 SEP 2000

     FILE 'HCAPLUS' ENTERED AT 13:08:55 ON 13 SEP 2000

     FILE 'REGISTRY' ENTERED AT 13:10:53 ON 13 SEP 2000

     FILE 'HCAPLUS' ENTERED AT 13:11:13 ON 13 SEP 2000

     FILE 'CAPLUS' ENTERED AT 13:11:58 ON 13 SEP 2000

     FILE 'HCAPLUS' ENTERED AT 13:12:10 ON 13 SEP 2000

     FILE 'MARPAT' ENTERED AT 13:13:57 ON 13 SEP 2000

     FILE 'CAPLUS' ENTERED AT 13:14:19 ON 13 SEP 2000

     FILE 'MARPAT' ENTERED AT 13:14:20 ON 13 SEP 2000

     FILE 'CAPLUS' ENTERED AT 13:14:54 ON 13 SEP 2000

     FILE 'MARPAT' ENTERED AT 13:15:06 ON 13 SEP 2000
L7               0 S  2(2W)DEOXY 2(2W)FLUORO(2W)RIBONUCLEOSIDE
L8               0 S NUCLEOSIED
L9               1 S NUCLEOSIDE
L10              0 S L9 AND L4

=> s nucleoside

NUCLEOSIDE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).
```

```
=> file hcaplus

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                          ENTRY     SESSION
FULL ESTIMATED COST                                       12.80      275.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                          ENTRY     SESSION
CA SUBSCRIBER PRICE                                        0.00      -12.78

FILE 'HCAPLUS' ENTERED AT 13:20:49 ON 13 SEP 2000
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1967 - 13 Sep 2000  VOL 133 ISS 12
FILE LAST UPDATED: 12 Sep 2000  (20000912/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

 This file supports REG1stRY for direct browsing and searching of
 all substance data from the REGISTRY file.  Enter HELP FIRST for
 more information.

Now you can extend your author, patent assignee, patent information,
and title searches back to 1907.  The records from 1907-1966 now have
this searchable data in CAOLD.  You now have electronic access to all
of CA: 1907 to 1966 in CAOLD and 1967 to the present in HCAPLUS on STN.

=> s nucleoside

NUCLEOSIDE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> e nucleoside

E1            1     NUCLEOSIDATIONS/BI
E2            2     NUCLEOSIDATO/BI
E3        32473 --> NUCLEOSIDE/BI
E4            1     NUCLEOSIDEA/BI
E5            1     NUCLEOSIDEACETIC/BI
E6            1     NUCLEOSIDEAMIDOPHOSPHITES/BI
E7            1     NUCLEOSIDEASE/BI
E8            2     NUCLEOSIDECARBOXYLATE/BI
E9            1     NUCLEOSIDECOMPONENT/BI
E10           1     NUCLEOSIDECYCLOPHOSPHATES/BI
E11           3     NUCLEOSIDEDI/BI
E12           7     NUCLEOSIDEDIPHOSPHATASE/BI

=> s e3 and l4

          32473 NUCLEOSIDE/BI
            186 L3
L11         115 NUCLEOSIDE/BI AND L4

=> s 2'-deoxy-2'-fluoro ribonucleoside
```

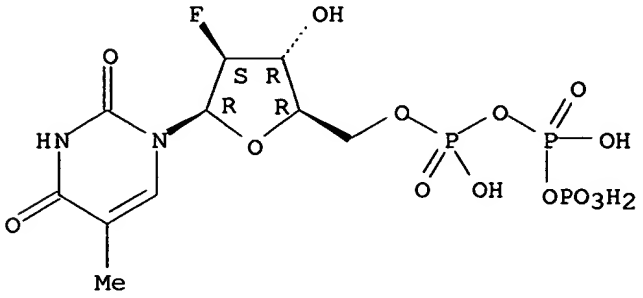
```
       5613964 2
         31827 'DEOXY'
       5613964 '2'
         55706 FLUORO
          2861 RIBONUCLEOSIDE
L12          0 2'-DEOXY-2'-FLUORO RIBONUCLEOSIDE
                 (2(W)'DEOXY'(W)'2'(W)FLUORO(W)RIBONUCLEOSIDE)

=> d l11 71-80 ibib abs hitstr


L11  ANSWER 71 OF 115  HCAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:        1987:168640  HCAPLUS
DOCUMENT NUMBER:         106:168640
TITLE:                   Inhibition of DNA primase by nucleoside
                         triphosphates and their arabinofuranosyl analogs
AUTHOR(S):               Parker, William B.; Cheng, Yung Chi
CORPORATE SOURCE:        Dep. Pharmacol., Univ. North Carolina, Chapel Hill,
                         NC, 27514, USA
SOURCE:                  Mol. Pharmacol. (1987), 31(2), 146-51
                         CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   DNA primase [64885-96-7] produces an RNA oligomer of approx. 10 bases,
     which is required by DNA polymerase .alpha. (EC 2.7.7.7) for the
     initiation of DNA synthesis. DNA primase was partially purified from
     acute lymphocytic leukemia cells from patients by using several
chromatog.
     columns. Poly(dT) and poly(dC), but not poly(dA) or poly(dG), were good
     templates for ribonucleoside triphosphate (rNTP)-dependent DNA synthesis
     (i.e., DNA primase activity), and they were used in the study of the
     effect of natural and arabinofuranosyl nucleoside triphosphates
     on DNA primase activity. The Km for GTP [86-01-1] in the poly(dC)
     primase assay was .apprx.175 .mu.M. All noncomplementary natural rNTPs
     and deoxyribonucleoside triphosphates (dNTPs) inhibited poly(dC) primase
     activity to a similar extent (Ki values of ATP [56-65-5] and CTP
     [65-47-4] were 610 and 517 .mu.M, resp.). 1-.beta.-D-
     Arabinofuranosylcytosine 5'-triphosphate (araCTP) [13191-15-6] and
     9-.beta.-D-arabinofuranosyladenine 5'-triphosphate (araATP) [3714-60-1]
     were more potent inhibitors of poly(dC) primase activity than were CTP
and
     ATP (Ki values were .apprx.125 .mu.M). AraCTP, araATP, CTP, and ATP
     inhibited DNA primase activity in a manner competitive with GTP. The
     concn. required to inhibit poly(dC) DNA primase activity by 50% was detd.
     for a no. of arabinofuranosyl nucleoside triphosphate analogs,
     and the relative potency of inhibition of DNA primase activity was as
     follows: rNTP = dNTP = 5-aza-dCTP [72052-96-1] < ara-5-azaCTP
     [98204-39-8] = araTTP [66097-68-5] = araATP = araCTP < 2-fluoro-araATP
     [74832-57-8] = 2'-azido-2'-deoxy-araCTP [59652-91-4] < 2'-fluoro-araTTP
     [79551-89-6] = 2'-fluoro-5-iodo-araCTP [79570-63-1] =
     2'-fluoro-5-methyl-araCTP [79570-62-0]. In the poly(dT) primase assay
     ATP did not follow classic Michaelis-Menten kinetics (ATP exhibited pos.
     cooperativity with a Hill coeff. of 2.0). However, this assay was very
     sensitive to araCTP (apparent Ki of 25 .mu.M). In summary, these expts.
     suggested that DNA primase is controlled by the levels of ribonucleoside
     triphosphates, and that the perturbation of these pools by any agent
could
     lead to the inhibition of DNA primase and thereby inhibit DNA synthesis.
     Furthermore, aranucleoside triphosphate analogs directly inhibited DNA
     primase, and it is possible that this effect may contribute to the
     cytotoxicity of these compds.
IT   79551-89-6
     RL: BIOL (Biological study)
        (DNA primase inhibition by, cytotoxic mechanism in relation to)
RN   79551-89-6  HCAPLUS
CN   2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-
```

[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

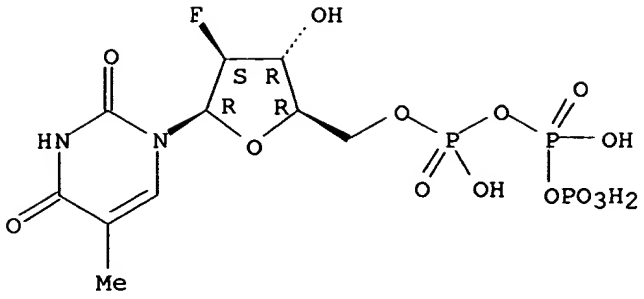


L11 ANSWER 72 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1987:152055 HCAPLUS
DOCUMENT NUMBER: 106:152055
TITLE: Human immunodeficiency virus reverse transcriptase. General properties and its interactions with **nucleoside** triphosphate analogs
AUTHOR(S): Cheng, Yung Chi; Dutschman, Ginger E.; Bastow, Kenneth F.; Sarngadharan, M. G.; Ting, Robert Y. C.
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: J. Biol. Chem. (1987), 262(5), 2187-9
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using affinity purified human immunodeficiency virus (HIV) reverse transcriptase, the reaction assay conditions were detd. The optimum incorporation of dTMP into the (rA)n(dT)10 template with HIV reverse transcriptase required 6 mM MgCl2 with 80 mM KCl. The template specificity of HIV reverse transcriptase was quite different from those of the human DNA polymerase-.gamma.-assocd. reverse transcriptase or avian virus reverse transcriptase. The preferential inhibition of HIV reverse transcriptase as compared to human DNA polymerase-.gamma.-assocd. reverse transcriptase was obsd. with several **nucleoside** analog triphosphates. The Ki values for thymidine triphosphate analogs with HIV reverse transcriptase were in the range 5-13 nM with decreasing effectiveness for 3'-fluoro > 3'-amino > 2',3'-dideoxy > 3'-azido groups. This study provided information on the structure-activity relations of the triphosphate analogs inhibitory effects on HIV reverse transcriptase vs. human DNA polymerase-.gamma.-assocd. reverse transcriptase, and the possible mechanisms of action of 3'-azidothymidine and the 2',3'-dideoxynucleosides, and also identified other **nucleoside** analogs for possible development as inhibitors of HIV.

IT **79551-89-6**
RL: BIOL (Biological study)
(reverse transcriptase of human immunodeficiency virus inhibition by)
RN 79551-89-6 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

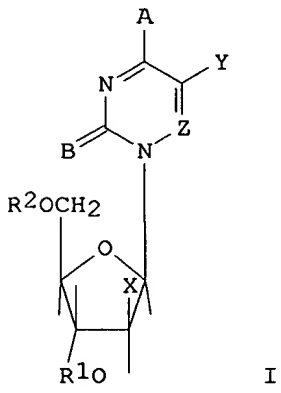
Absolute stereochemistry.



L11 ANSWER 73 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1987:113538 HCAPLUS
DOCUMENT NUMBER: 106:113538
TITLE: Anti-herpes virus compositions containing 5-substituted (1,2'-deoxy-2'-substituted .beta.-D-arabinofuranosyl)pyrimidine nucleosides
INVENTOR(S): Lopez, Carlos; Watanabe, Kyoichi A.; Reichman, Uri; Fox, Jack J.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: U.S., 11 p. Cont. of U.S. Ser. No. 366,104, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4594339	A	19860610	US 1984-621875	19840618
PRIORITY APPLN. INFO.:			US 1982-366104	19820406

GI



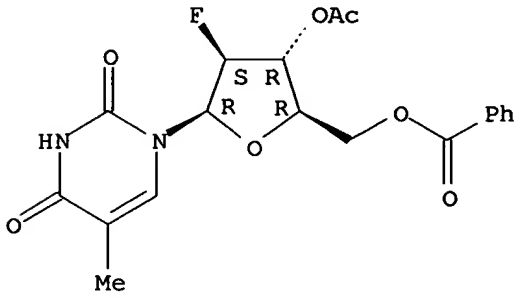
I

AB The title compds. (I; A = OR3, SR3, NR3R4, or NH-acyl; R3, R4 = H, C1-7 alkyl, aralkyl, aryl; B = O, S; X = H, alkylsulfonyl, arylsulfonyl; Y = halo, NH2, monoalkyl, etc.; Z = methyne, N; R1, R2 = H, acyl, aroyl) are effective in controlling herpes virus. Thus, 88 I compds. are claimed, and the prepns. of some of them are described. The inhibitory activities of some I compds. such as 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine against herpes simplex virus type 1 and 2 were demonstrated in vitro.

IT **69124-04-5**
RL: RCT (Reactant)

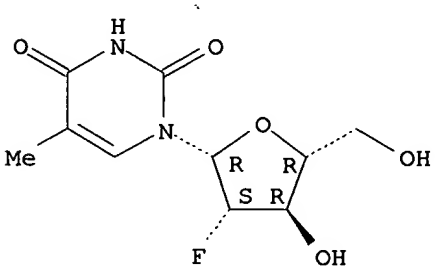
(deblocking and deacetylation of)
RN 69124-04-5 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(3-O-acetyl-5-O-benzoyl-2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **69256-17-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antiherpes virus activity of)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione,
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of

L11 ANSWER 74 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1987:60841 HCAPLUS
DOCUMENT NUMBER: 106:60841
TITLE: Comparative efficacy of three 2'-fluoropyrimidine nucleosides and 9-(1,3-dihydroxy-2-propoxymethyl)guanine (BW B759U) against pseudorabies and equine rhinopneumonitis virus infection in vitro and in laboratory animals
AUTHOR(S): Rollinson, Elizabeth A.
CORPORATE SOURCE: Coppers Anim. Health Ltd., Berkhamsted/Hertfordshire, HP4 2QE, UK
SOURCE: Antiviral Res. (1987), 7(1), 25-33
CODEN: ARSRDR; ISSN: 0166-3542
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 3 2'-fluoropyrimidine nucleosides 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) [69123-90-6], 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodouracil (FIAU) [69123-98-4], and 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil (FMAU) [**69256-17-3**], showed high activity in RK13 monolayers against equine rhinopneumonitis virus, (EHV-1), Aujeszky's disease virus (SHV-1, pseudorabies), and infectious bovine rhinotracheitis

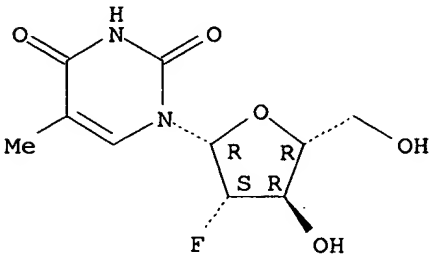
virus (1BR, BHV-1). The activity of these compds. was compared with 9-(1,3-dihydroxy-2-propoxymethyl)guanine (BW B759U, DHPG) in 2 lab. animal disease models: EHV-1-induced hepatitis in hamsters and SHV-1-induced encephalitis in mice. All the compds., provided from 3 to 5 h pre-infection for 5 days, were effective in preventing EHV-1 mortality (at 3-5 mg/kg per day) and in significantly reducing SHV-1 mortality (at 60 mg/kg per day). While FIAU had the greatest activity in vitro, FMAU tended to be more potent in vivo. The reasons for these differences between relative in vitro and in vivo activities are briefly discussed.

IT **69256-17-3**, 1-(2-Deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral activity of, against pseudorabies and equine rhinopneumonitis virus)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 75 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1987:18982 HCAPLUS

DOCUMENT NUMBER: 106:18982

TITLE: Nucleosides. 139. Synthesis and anticytomegalovirus and antiherpes simplex virus activity of 5'-modified analogs of 2'-fluoroarabinosylpyrimidine nucleosides

AUTHOR(S): Harada, Kazuho; Matulic-Adamic, Jasenka; Price, Richard W.; Schinazi, Raymond F.; Watanabe, Kyoichi A.; Fox, Jack J.

CORPORATE SOURCE: Grad. Sch. Med. Sci., Cornell Univ., New York, NY, 10021, USA

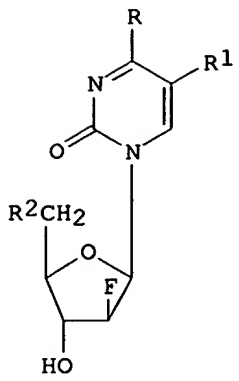
SOURCE: J. Med. Chem. (1987), 30(1), 226-9
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 106:18982

GI



I

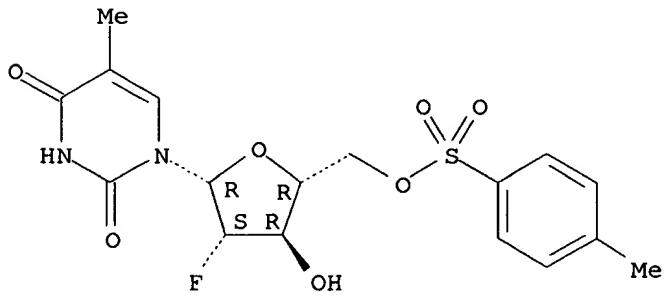
AB In order to det. if modification of the 5'-position reduces or abolishes the antiviral activity of the title nucleosides (I, R = NH2, OH; R1 = iodo, Me; R2 = OH) against human cytomegalovirus (HCMV) and herpes simplex virus (HSV), I (R2 = H, SH, NH2) were prepd. I (R2 = H) were prepd. by catalytic hydrogenation of I (R2 = iodo) followed by reiodination at C-5. I (R2 = iodo) were inactive against HCMV, indicating that the conversion to 5'-phosphate by cellular enzymes is a requirement for antiviral activity against this virus. Treatment of I (R2 = O3SC6H4Me-4) with LiN3 in DMF afforded I (R2 = N3). Catalytic hydrogenation of I (R = OH, R1 = Me, R2 = N3) afforded I (R = OH, R1 = Me, R2 = NH2), whereas I (R = NH2, R1 = iodo, R2 = NH2) was obtained by treatment of I (R = NH2, R1 = iodo, R2 = N3) with Ph3P in pyridine. I (R2 = SH) were prepd. by treatment of 5'-O-tosyl-3'-O-acetyl nucleosides with KSAc followed by deacetylation. I (R = OH, R1 = Me, R2 = NH2) was the only compd. that showed good activity against HSV-1 and HSV-2 in vitro. However, this compd. was less potent and had a lower therapeutic index than I (R = R2 = OH, R1 = Me).

IT **105281-02-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with azide)

RN 105281-02-5 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-[(4-methylphenyl)sulfonyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

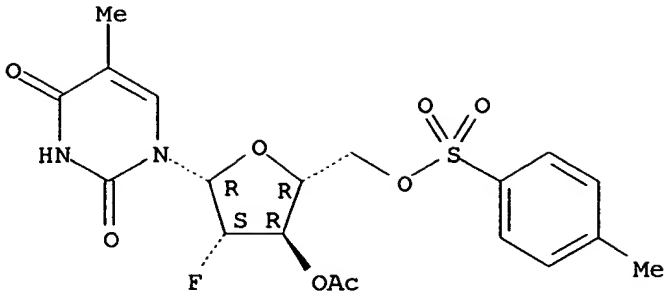


IT **105281-16-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with thioacetate)

RN 105281-16-1 HCAPLUS

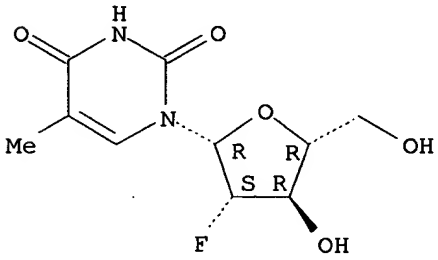
CN 2,4(1H,3H)-Pyrimidinedione, 1-[3-O-acetyl-2-deoxy-2-fluoro-5-O-[(4-methylphenyl)sulfonyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **69256-17-3**
RL: RCT (Reactant)
(tosylation of)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione,
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



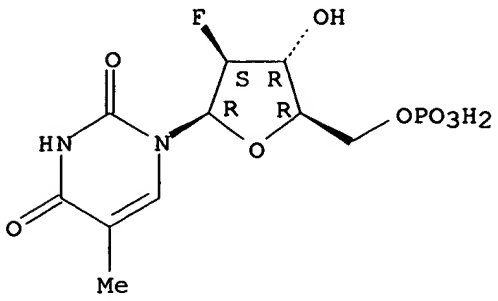
L11 ANSWER 76 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:618182 HCAPLUS
DOCUMENT NUMBER: 105:218182
TITLE: Quantitative determination of antiviral **nucleoside** analog in DNA
AUTHOR(S): Chen, Ming S.; Van Nostrand, Mary; Oshana, Scott C.
CORPORATE SOURCE: Pharm. Res. Dev. Div., Bristol-Myers Co., Syracuse, NY, 13221-4755, USA
SOURCE: Anal. Biochem. (1986), 156(2), 300-4
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A technique for the anal. of the amt. of an antiviral **nucleoside** analog incorporated into DNA utilizing enzymic digestion of DNA, followed by HPLC is described. The cells or tissue samples were treated with perchloric acid to inactivate the nucleases, then digested with pronase in the presence of EDTA. DNA was purified by CsCl centrifugation followed by Sephadex chromatog. and treatment with DNase 1 and venom phosphodiesterase. The deoxyribonucleoside monophosphates and the monophosphate of the **nucleoside** analog liberated from DNA were sepd. and quantitated by HPLC anal. and measurement of radioactivity. This assay is more sensitive, specific, and precise than the detn. of DNA d. shift. It is also applicable for **nucleoside** analogs which do not change the d. of DNA either because of their structure or their very small degree of incorporation.

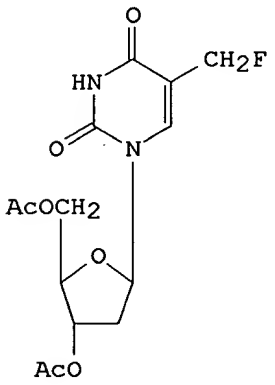
IT **94344-82-8**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in cells and tissues by HPLC after enzymic digestion)

RN 94344-82-8 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-5-O-phosphono-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 77 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:591546 HCAPLUS
DOCUMENT NUMBER: 105:191546
TITLE: Nucleosides. 138. Synthesis and biological activity of .alpha.-monofluoro- and .alpha.,.alpha.-difluoro-thymine nucleosides
AUTHOR(S): Matulic-Adamic, Jasenka; Watanabe, Kyoichi A.; Price, Richard W.
CORPORATE SOURCE: Grad. Sch. Med. Sci., Cornell Univ., New York, NY, 10021, USA
SOURCE: Chem. Scr. (1986), 26(1), 127-34
CODEN: CSRPB9; ISSN: 0004-2056
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:191546
GI



I

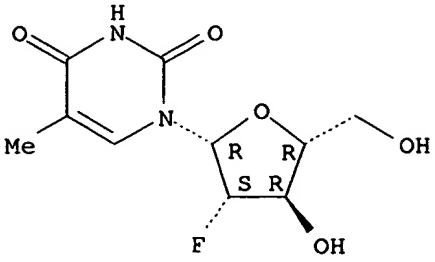
AB Several title nucleosides were prepd. and their antiherpes activity detd. For example, a soln. of 3',5'-di-O-acetylthymidine in CCl4 was refluxed with Br (irradn. 500 W UV lamp) and the resultant .alpha.-bromothymidine diacetate treated with AgF in MeCN to give .alpha.-fluorothymidine I. Inhibitory concn. of I against HSV-1 and HSV-2 was >100 .mu.M and the toxic concn. was 1000 .mu.M.

IT **69256-17-3**
RL: RCT (Reactant)
(acetylation of)

RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-

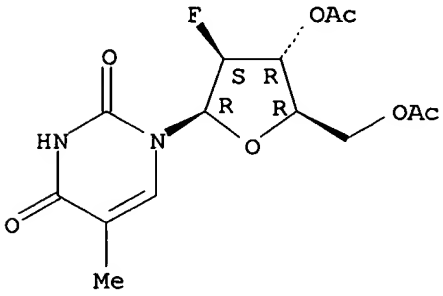
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



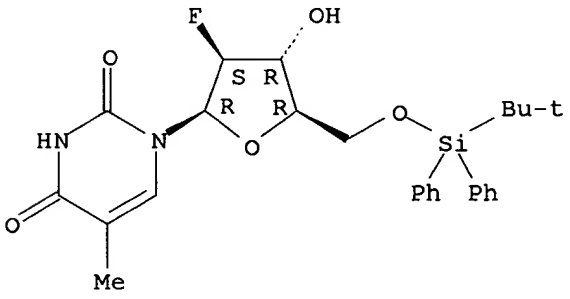
IT **104904-75-8P 104904-80-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and bromination of)
RN 104904-75-8 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(3,5-di-O-acetyl-2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



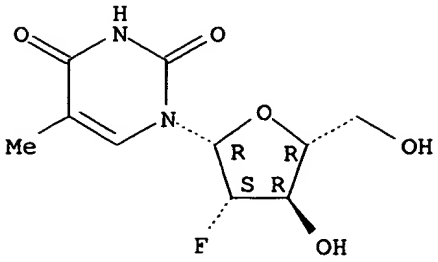
RN 104904-80-5 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-5-O-[(1,1-dimethylethyl)diphenylsilyl]-2-fluoro-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **69256-17-3**
RL: RCT (Reactant)
(tert-butyldiphenylsilylation of)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



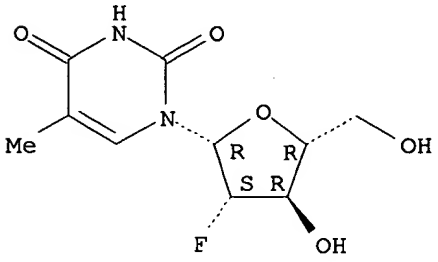
L11 ANSWER 78 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:490825 HCAPLUS
DOCUMENT NUMBER: 105:90825
TITLE: Susceptibility of varicella-zoster virus to thymidine analogs
AUTHOR(S): Machida, Haruhiko
CORPORATE SOURCE: Res. Lab., Yamasa Shoyu Co., Ltd., Choshi, 288, Japan
SOURCE: Biken J. (1986), 29(1), 1-6
CODEN: BKNJA5; ISSN: 0006-2324
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ten strains of varicella-zoster virus (VZS) were tested for susceptibility to 17 **nucleoside** analogs by a plaque redn. assay using human embryonic lung fibroblast cells. The compds. employed were 5-substituted arabinosyluracils and 2'-deoxyuridines, 2'-fluoro-arabinosylpyrimidines (F-araPyr) and acyclovir [59277-89-3]. In terms of the 50% plaque redn. dose (PD50), 4- to 40-fold difference were found between the 10 strains of VZV in susceptibilities to each compd. VZV was highly susceptible to 5-halogenovinyl-arabinosyluracils (XV-araUs); the PD50 values of these compds. were less than 0.001 .mu.g/mL. VZV was much more susceptible than either HSV type 1 or type 2 to 5-ethyl-2'-deoxyuridine [15176-29-1], 5-ethylarabinosyluracil [70020-72-3], and acyclovir.

IT **69256-17-3**
RL: BIOL (Biological study)
(varicella-zoster virus susceptibility to)

RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 79 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:472131 HCAPLUS
DOCUMENT NUMBER: 105:72131
TITLE: Enzymology and pathogenicity in mice of a herpes simplex virus type 1 mutant resistant to

2'-fluoro-2'-deoxy-1-.beta.-D-arabinofuranosyl-5-iodocytosine

AUTHOR(S): Colacino, Joseph; Brownridge, Elizabeth; Greenberg, Nancy; Lopez, Carlos

CORPORATE SOURCE: Lab. Herpesvirus Infect., Mem. Sloan Kettering Cancer Cent., New York, NY, 10021, USA

SOURCE: Antimicrob. Agents Chemother. (1986), 29(5), 877-82
CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal

LANGUAGE: English

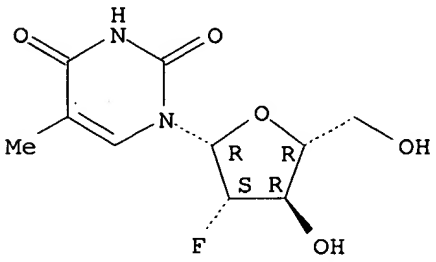
AB The deoxypyrimidine **nucleoside** analog 2-fluoro-2'-deoxy-1-.beta.-D-arabinofuranosyl-5-iodocytosine (FIAC) [69123-90-6] is a potent and selective inhibitor of herpes simplex virus type I in vitro. Isopycnog. anal. demonstrated that 1 .mu.M FIAC inhibited herpes simplex virus DNA replication by more than 95% but inhibited cellular DNA replication by only 32%. Mutant herpes simplex virus type 1 selected resistant to FIAC displayed linked resistance to other **nucleoside** analogs, including arabinosylthymine [605-23-2] and acyclovir [59277-89-3]. Lysates derived from Vero cells infected with FIAC-resistant virus showed markedly lower levels of thymidine kinase [9002-06-6] activity and were unable to phosphorylate selectively arabinosylthymine or FIAC, in contrast to lysates from the cells infected with wild-type herpes simplex virus type 1. Drug-resistant virus displayed a 6,000-fold decrease in pathogenicity when inoculated i.p. into genetically susceptible A/J mice. These results indicate that resistance to deoxypyrimidine **nucleoside** analogs is due, at least in part, to alterations in viral thymidine kinase and is accompanied by decreased pathogenicity in vivo.

IT **69256-17-3**
RL: BIOL (Biological study)
(herpes virus resistant to fluorodeoxyarabinofuranosyliodocytosine sensitivity to)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 80 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1986:180200 HCAPLUS

DOCUMENT NUMBER: 104:180200

TITLE: Treatment of hepatitis with pyrimidine nucleosides

PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA

SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

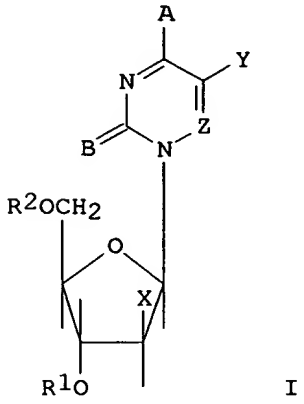
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 60252418	A2	19851213	JP 1985-44479	19850306
AU 8539534	A1	19850912	AU 1985-39534	19850305
AU 575918	B2	19880811		
HU 39189	A2	19860828	HU 1985-827	19850305
HU 198393	B	19891030		
US 4666892	A	19870519	US 1986-828569	19860210

PRIORITY APPLN. INFO.: US 1984-586729 19840306

GI



I

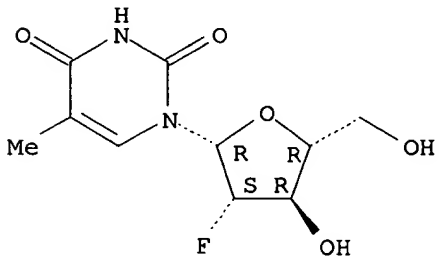
AB 5-Substituted 1-(2'-deoxy-2'-substituted-.beta.-D-arabinofuranosyl)pyrimidines I, where A = OR3, SR3, NR3R4, or acylamido; R3, R4 = H, C1-7 alkyl, aralkyl, or aryl; B = O or S; X = halo, alkylsulfonyl, or arylsulfonyl; Y = halo, amino, alkyl, etc.; Z = C or N; R1, R2 = H, acyl, or aroyl, are effective in treatment of hepatitis B virus infection. The efficacies of several compds. such as 2'-fluoro-2'-deoxyarabinosyl-5-iodocytosine were shown in patients.

IT **69256-17-3**
RL: BIOL (Biological study)
(hepatitis treatment with)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d l11 82-90 ibib abs hitstr

L11 ANSWER 82 OF 115 HCAPLUS COPYRIGHT 2000 ACS

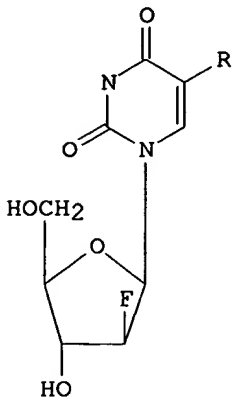
ACCESSION NUMBER: 1986:179765 HCAPLUS

DOCUMENT NUMBER: 104:179765

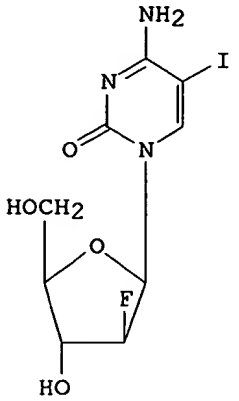
TITLE: Preclinical investigations of FIAU, an anti-herpes agent

AUTHOR(S): McLaren, C.; Chen, M. S.; Barbhaiya, R. H.; Buroker,

R. A.; Oleson, F. B.
CORPORATE SOURCE: Bristol-Myers Co., Syracuse, NY, 13221-4755, USA
SOURCE: Int. Congr. Ser. - Excerpta Med. (1985), 667(Herpes Viruses Virus Chemother.), 57-61
CODEN: EXMDA4; ISSN: 0531-5131
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, R=I
III, R=Me

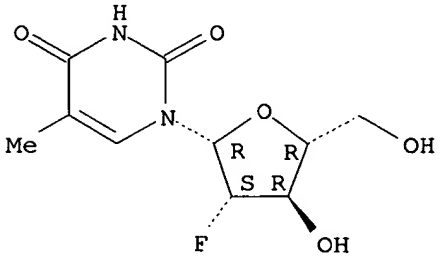


II

AB The pharmacol. of FIAU (I) [69123-98-4] as an anti-herpes agent is described in relation to that of FIAC (II) [69123-90-6] and FMAU (III) [**69256-17-3**]. The mechanism of action of I is dependent on selective inhibition of viral thymidine kinase [9002-06-6]. The I monophosphate [99891-31-3] and III monophosphate [**94344-82-8**] had better affinities for cellular thymidylate kinase [9014-43-1] than for herpes simplex virus thymidine/thymidylate kinases. However, II monophosphate [99876-43-4] had poor affinities for either the cellular or herpes simplex virus enzymes. In cells exposed to 14C-labeled II, I monophosphate was the major metabolite, indicating that II is converted to the more active agent, I. I appeared to have good activity, but it had cardiotoxic and myelosuppressive activities.

IT **69256-17-3**
RL: BIOL (Biological study)
(herpes virus inhibition by, thymidine kinase inhibition in, toxicity in relation to)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



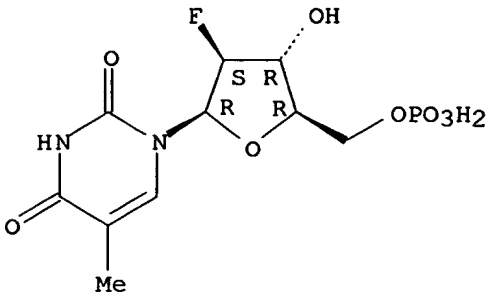
IT **94344-82-8**
RL: BIOL (Biological study)

(thymidylate kinase inhibition by, herpes virus inhibition in relation to)

RN 94344-82-8 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-5-O-phosphono-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 83 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1986:81578 HCAPLUS

DOCUMENT NUMBER: 104:81578

TITLE: Activities of 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine and its metabolites against herpes simplex virus types 1 and 2 in cell culture and in mice infected intracerebrally with herpes simplex virus type 2

AUTHOR(S): Schinazi, Raymond F.; Fox, Jack J.; Watanabe, Kyoichi A.; Nahmias, Andre J.

CORPORATE SOURCE: Veterans Adm. Med. Cent., Atlanta, GA, 30303, USA

SOURCE: Antimicrob. Agents Chemother. (1986), 29(1), 77-84
CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal

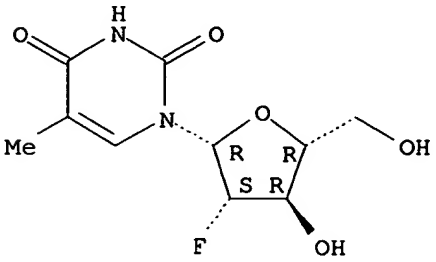
LANGUAGE: English

AB As measured by plaque and yield redn. assays, several metabolites of 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) were highly active against herpes simplex virus types 1 and 2. These metabolites included the 2'-deoxy-2'-fluoroarabinosyl derivs. of 5-iodouracil, cytosine, uracil, and thymine. In mice inoculated intracerebrally with herpes simplex virus type 2, the relative order of potency of these compds. and known antiviral drugs were as follows: 2'-fluoro-5-methylarabinosyluracil (FMAU) [**69256-17-3**] .mchgt. 2'-fluoro-5-iodoarabinosylcytosine (FIAC) [69123-90-6] .apprxeq. 2'-fluoro-5-iodoarabinosyluracil (FIAU) [69123-98-4] > acyclovir .apprxeq. vidarabine .mchgt. 2'-fluoroarabinosylcytosine (FAC) [56632-83-8] .apprxeq. 2'-fluoroarabinosyluracil (FAU) [69123-94-0]. One of the main metabolites of FMAU, 2'-fluoro-5-hydroxymethylarabinosyluracil [94817-51-3], was essentially inactive in vivo. FIAC-, FIAU-, FMAU-, FAC-, and FAU-resistant herpes simplex virus variants prepd. in cell culture were found to be (i) devoid of viral thymidine kinase [9002-06-6], (ii) cross-resistant to one another and resistant to drugs requiring viral thymidine kinase for activation, and (iii) sensitive to vidarabine or phosphonoformate. These results indicate that FIAC, FIAU, and FMAU require the virally encoded thymidine kinase for activation and suggest that the antiviral activity of FAU and FAC in cell cultures is also mediated by this enzyme. The interaction of the fluoroarabinosylpyrimidine nucleosides with herpes simplex virus thymidine kinase in a cell-free system is also described.

IT **69256-17-3**
RL: BIOL (Biological study)

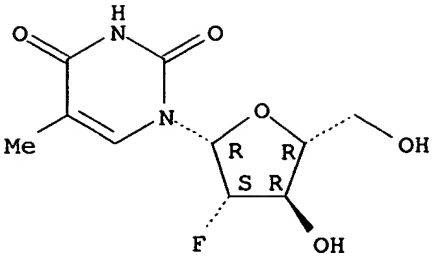
(herpes simplex virus type 2 inhibition by)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione,
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 84 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:81562 HCAPLUS
DOCUMENT NUMBER: 104:81562
TITLE: Selective inhibition of the proliferation of herpes simplex virus type 1 thymidine kinase gene-transformed murine mammary FM3A carcinoma cells by (E)-5-(2-bromovinyl)-2'-deoxyuridine and related compounds
AUTHOR(S): Balzarini, J.; De Clercq, E.; Ayusawa, D.; Shimizu, K.; Seno, T.
CORPORATE SOURCE: Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.
SOURCE: Nucleic Acids Symp. Ser. (1985), 16(Symp. Nucleic Acids Chem., 13th), 283-6
CODEN: NACSD8; ISSN: 0261-3166
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mouse mammary carcinoma FM3A cells deficient in thymidine kinase [9002-06-6] were transformed by a cloned gene for herpes simplex virus type 1 thymidine kinase. Among several antiherpetic **nucleoside** analog, (E)-5-(2-bromovinyl)-2'-deoxyuridine [69304-47-8], (E)-5-(2-iodovinyl)-2'-deoxyuridine [69304-48-9], and (E)-5-(2-bromovinyl)-2'-deoxycytidine [74131-09-2] inhibited the growth of the transformed cells at concns. 5000- to 20000-fold lower than those required to inhibit the growth of their corresponding wild-type cells. The selective inhibitory action of these compds. was due to a specific phosphorylation by the viral thymidine kinase. From the transformed cells, thymidine-auxotrophic mutants that are deficient in thymidylate synthase were isolated. These mutant cell lines should prove useful in elucidating the mechanism of action of the antiherpetic **nucleoside** analogs.
IT **69256-17-3**
RL: BIOL (Biological study)
(herpes simplex virus type 1 thymidine kinase gene-transformed mammary carcinoma cell growth inhibition by)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione,
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

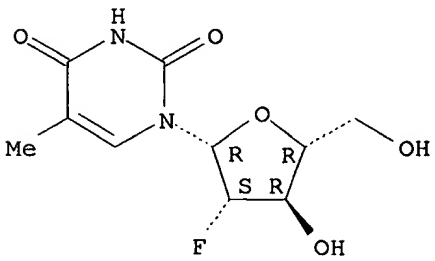


L11 ANSWER 85 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:45371 HCAPLUS
DOCUMENT NUMBER: 104:45371
TITLE: Effects of **nucleoside** analogs in inhibition of Epstein-Barr virus
AUTHOR(S): Lin, J. C.; Nelson, D. J.; Lambe, C. U.; Choi, E. I.; Pagano, J. S.
CORPORATE SOURCE: Lineberger Cancer Res. Cent., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: Int. Congr. Ser. - Excerpta Med. (1985), 667(Herpes Viruses Virus Chemother.), 225-7
CODEN: EXMDA4; ISSN: 0531-5131
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The relative antiviral potency of several **nucleoside** analogs against Epstein-Barr virus infection in P3HR-1 cells was 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine (I) [69123-90-6] = 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodouracil (II) [69123-98-4] > 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-thymine (III) [**69256-17-3**] > BW B759U (IV) [82410-32-0] > E-5-(2-bromovinyl)-2'-deoxyuridine (V) [69304-47-8] > acyclovir (VI); the relative therapeutic efficacy (ratio of cytotoxicity to antiviral potency) was V > IV > I > VI > II > III. IV was rapidly and markedly phosphorylated by virus-infected Raji cells; this effect was 100-fold greater than for VI. The results are discussed with respect to the prolonged inhibitory action of the **nucleoside** analogs against Epstein-Barr virus replication.

IT **69256-17-3**
RL: BIOL (Biological study)
(Epstein-Barr virus infection inhibition by)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



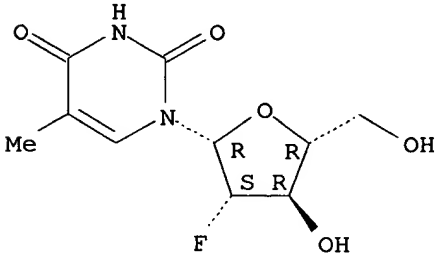
L11 ANSWER 86 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:45345 HCAPLUS

L11 ANSWER 87 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:14570 HCAPLUS
DOCUMENT NUMBER: 104:14570
TITLE: Human cytomegalovirus-induced DNA polymerase and its interaction with the triphosphates of 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil, -5-iodocytosine, and -5-methylcytosine
AUTHOR(S): Mar, Eng Chun; Chiou, Jwo Farn; Cheng, Yung Chi; Huang, Eng Shang
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: J. Virol. (1985), 56(3), 846-51
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human cytomegalovirus-induced DNA polymerase [9012-90-2] and cellular DNA polymerase .alpha. were purified by successive chromatog. on DEAE-cellulose, phosphocellulose, heparin agarose, and single-stranded DNA agarose columns. The purified virus-induced DNA polymerase was resolved to 2 polypeptides corresponding to mol. wts. of 140,000 and 58,000, as analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Virus-induced DNA polymerase and cellular .alpha. polymerase were examd. for their sensitivities to the triphosphates of 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil (FMAUTP) [**69256-17-3**], -5-iodocytosine (FIACTP) [69123-90-6], and -5-methylcytosine (FMACTP) [78636-53-0]. The inhibitive effects of these triphosphates on the DNA polymerases were competitive with regard to the natural substrates; thus FMAUTP completes with dTTP [365-08-2], and FIACTP and FMACTP complete with dCTP [2056-98-6]. The inhibition consts. (Ki) for FMAUTP, FIACTP, and FMACTP of virus-induced DNA polymerase are 0.06, 0.30, and 0.47 .mu.M, resp. Cellular DNA polymerase .alpha. is much less sensitive to these inhibitors, and its Ki values for FMAUTP, FIACTP, and FMACTP are 0.45, 3.10, and 2.90 .mu.M, resp. In addn., human cytomegalovirus-induced DNA polymerase, but not cellular DNA polymerase .alpha., can utilize these analog triphosphates as alternate substrates for their corresponding natural deoxyribonucleoside triphosphates in in vitro DNA synthesis.

IT **69256-17-3**
RL: BIOL (Biological study)
(DNA polymerase of cell and induced by human cytomegalovirus response to, antiviral mechanism in relation to)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 88 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:605545 HCAPLUS
DOCUMENT NUMBER: 103:205545
TITLE: Ab initio studies of the antiviral drug

9-(1,3-dihydroxy-2-propoxymethyl)guanine, acyclovir, and two 2'-fluoropyrimidine nucleosides

AUTHOR(S): Smee, Donald F.; Campbell, Nancy L.; Matthews, Thomas R.

CORPORATE SOURCE: Syntex Res., Mountain View, CA, 94043, USA

SOURCE: Antiviral Res. (1985), 5(5), 259-67
CODEN: ARSRDR; ISSN: 0166-3542

DOCUMENT TYPE: Journal

LANGUAGE: English

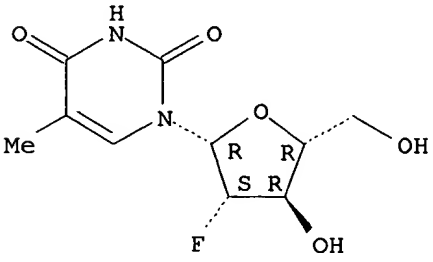
AB 9-(1,3-Dihydroxy-2-propoxymethyl)guanine (DHPG) [82410-32-0], was evaluated in cell culture and in animals for its inhibitory effect on herpes simplex viruses. Compds. used for comparison included acyclovir [59277-89-3], 2'-fluoro-2'-deoxy-5-iodoarabinofuranosylcytosine (FIAC) [69123-90-6], and 2'-fluoro-2'-deoxy-5-methylarabinofuranosyluracil (FMAU) [**69256-17-3**]. In plaque-redn. assays DHPG, acyclovir, FIAC, and FMAU were inhibitory to 6 herpes types 1 and 2 virus strains at concns. of 0.2-2.4 .mu.M. These concns. were much lower than those required to inhibit Vero cell proliferation. In guinea pig vaginal infections, DHPG provided significantly greater inhibition of herpetic lesions than did acyclovir. In a herpes type 2 infection model in mice, DHPG, and FMAU were active at 5 mg/kg, whereas acyclovir and FIAC showed no statistically significant effect at 80 mg/kg. In a herpes type 1 encephalitis model, DHPG and FMAU were active at doses <10 mg/kg, with FMAU being about 4 times more potent than DHPG in that model.

IT **69256-17-3**
RL: BIOL (Biological study)
(antiherpes virus activity of, (dihydroxypropoxymethyl)guanine in comparison with)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 90 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1985:523851 HCAPLUS

DOCUMENT NUMBER: 103:123851

TITLE: Fluorocarbohydrates in synthesis. An efficient synthesis of 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodouracil (.beta.-FIAU) and 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)thymine (.beta.-FMAU)

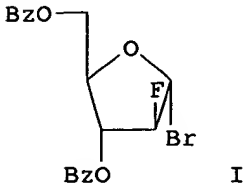
AUTHOR(S): Tann, Chou H.; Brodfuehrer, Paul R.; Brundidge, Steven P.; Sapino, Chester, Jr.; Howell, Henry G.

CORPORATE SOURCE: Pharm. Res. Dev. Div., Bristol-Myers, Syracuse, NY, 13221-4755, USA

SOURCE: J. Org. Chem. (1985), 50(19), 3644-7
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 103:123851
GI



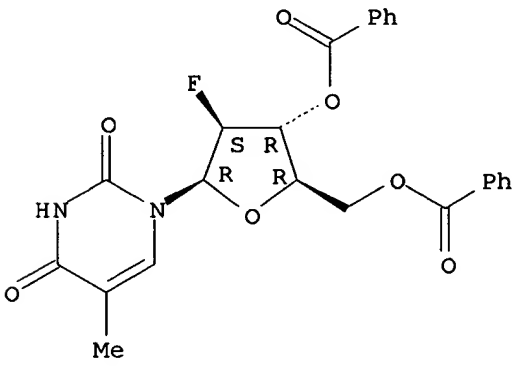
I

AB A 4-step, highly efficient synthesis of .beta.-FIAU and .beta.-FMAU is reported. 2-Deoxy-2-fluoro-1,3,5-tri-O-benzoyl-.alpha.-D-arabinofuranose was prepd. form 1,3,5-tri-O-benzoyl-.alpha.-D-ribofuranose, by fluorination of the corresponding 2-O-(imidazolylsulfonyl) deriv. in 63% yield. The use of anomerically pure bromide I for coupling to the **nucleoside** base results in higher yields of the desired .beta.-nucleosides.

IT **97614-47-6P 97614-48-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and debenzoylation of)

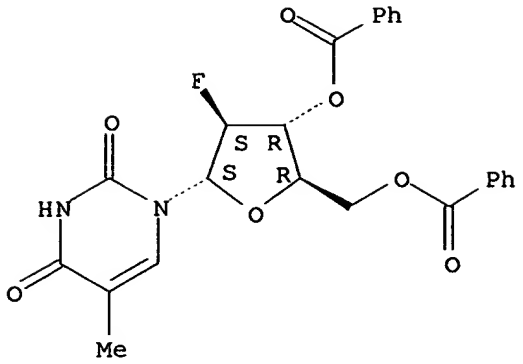
RN 97614-47-6 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione,
1-(3,5-di-O-benzoyl-2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



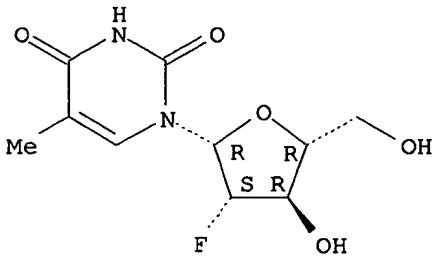
RN 97614-48-7 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione,
1-(3,5-di-O-benzoyl-2-deoxy-2-fluoro-.alpha.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



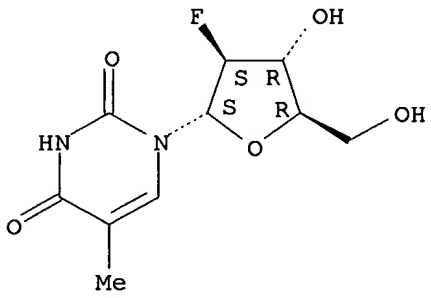
IT **69256-17-3P 97672-34-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione,
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 97672-34-9 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.alpha.-D-
arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L11 ANSWER 91 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:481377 HCAPLUS
DOCUMENT NUMBER: 103:81377
TITLE: Murine mammary FM3A carcinoma cells transformed with the herpes simplex virus type 1 thymidine kinase gene are highly sensitive to the growth-inhibitory

properties of (E)-5-(2-bromovinyl)-2'-deoxyuridine and related compounds

AUTHOR(S): Balzarini, J.; De Clercq, E.; Ayusawa, D.; Seno, T.

CORPORATE SOURCE: Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.

SOURCE: FEBS Lett. (1985), 185(1), 95-100
CODEN: FEBLAL; ISSN: 0014-5793

DOCUMENT TYPE: Journal

LANGUAGE: English

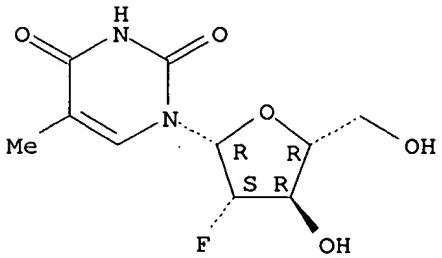
AB Murine mammary carcinoma (FM3A TK-/HSV-1 TK+) cells, which are thymidine kinase (TK) [9002-06-6]-deficient but have been transformed with the herpes simplex virus type 1 (HSV-1) TK gene, are inhibited in their growth by (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVDU) [69304-47-8], (E)-5(2-iodovinyl)-2'-deoxyuridine [69304-48-9], and (E)-5-(2-bromovinyl)-2'-deoxycytidine [74131-09-2] at 0.5, 0.5 and 0.8 ng/mL, resp. (i.e., a concn. 5000-20,000-fold lower than that required to inhibit the growth of the corresponding wild-type FM3A/0 cells). Hence, transformation of tumor cells with the HSV-1 TK gene makes them particularly sensitive to the cytostatic action of BVDU and related compds.

IT **69256-17-3**
RL: PRP (Properties)
(cytotoxicity of, to herpes virus-transformed carcinoma cell, thymidine kinase in relation to)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 92 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1985:447858 HCAPLUS

DOCUMENT NUMBER: 103:47858

TITLE: Comparative efficacy and selectivity of some **nucleoside** analogs against Epstein-Barr virus

AUTHOR(S): Lin, Jung Chung; Smith, M. Carolyn; Pagano, Joseph S.

CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA

SOURCE: Antimicrob. Agents Chemother. (1985), 27(6), 971-3
CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal

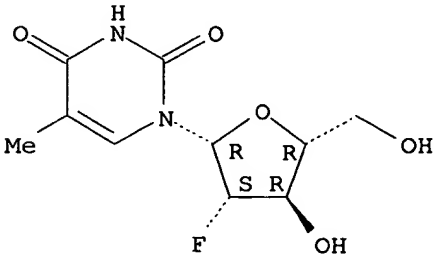
LANGUAGE: English

AB The effects of (2-deoxy-2-fluro-.beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) [69123-90-6], 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyluridine (FMAU) [**69256-17-3**], 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodouridine (FIAU) [69123-98-4], (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVdU) [69304-47-8], and 9-(1,3-dihydroxy-2-propoxymethyl)guanine (DHPG or BW B759U) [82410-32-0] on the replication

of Epstein-Barr virus (EBV) in vitro were evaluated and compared with that of acyclovir (ACV). The relative potencies of these drugs, on the basis of anti-EBV activity, were: FIAC = FIAU > FMAU > DHPG > BVdU > ACV; on the basis of the therapeutic index they were: BVdU > DHPG > FIAC > ACV > FIAU > FMAU. Differential inhibition of EBV-assocd. polypeptides by these drugs was obsd.

IT **69256-17-3**
RL: BIOL (Biological study)
(Epstein-Barr virus inhibition by)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

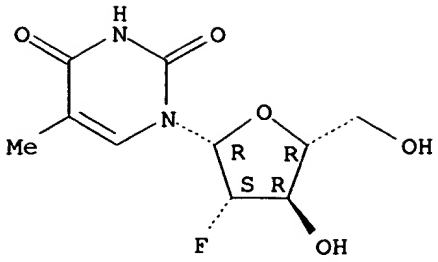


L11 ANSWER 93 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:416283 HCAPLUS
DOCUMENT NUMBER: 103:16283
TITLE: Incorporation of 5-substituted pyrimidine **nucleoside** analogs into DNA of a thymidylate synthetase-deficient murine FM3A carcinoma cell line
AUTHOR(S): Balzarini, Jan; De Clercq, Erik; Ayusawa, Dai; Seno, Takeshi
CORPORATE SOURCE: Rega Inst. Med. Res., Univ. Leuven, Louvain, B-3000, Belg.
SOURCE: Methods Find. Exp. Clin. Pharmacol. (1985), 7(1), 19-28
CODEN: MFEPDX; ISSN: 0379-0355
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A thymidylate (dTMP) synthetase [9031-61-2]-deficient murine mammary carcinoma cell line (FM3A/T5) which is auxotrophic for thymidine (dThd) was developed as a system with which to screen pyrimidine **nucleoside** analogs for their ability to sustain cell growth and, apparently, be incorporated into host-cell DNA. A no. of 5-substituted derivs. of 2'-deoxyuridine (dUrd) and 2'-deoxycytidine (dCyd) were found to stimulate growth, the dCyd derivs. apparently being deaminated to their dUrd analogs before incorporation into DNA. None of the 5-substituted derivs. of 1-.beta.-D-arabinofuranosyluracil or 1-.beta.-D-arabinofuranosylcytosine were growth-stimulating.

IT **69256-17-3**
RL: PROC (Process)
(DNA incorporation of, in thymidylate synthetase-deficient murine mammary carcinoma cell line)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

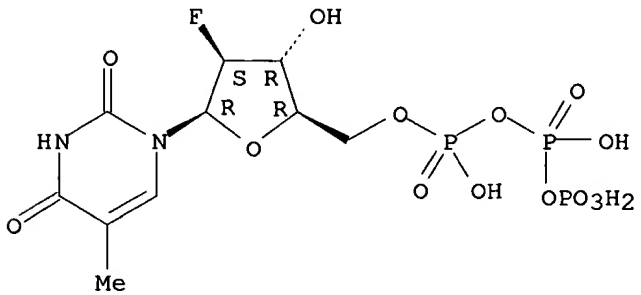


L11 ANSWER 94 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:201003 HCAPLUS
DOCUMENT NUMBER: 102:201003
TITLE: Interaction of Epstein-Barr virus DNA polymerase and 5'-triphosphates of several antiviral **nucleoside** analogs
AUTHOR(S): Chiou, Jwo Farn; Cheng, Yung Chi
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: Antimicrob. Agents Chemother. (1985), 27(3), 416-18
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 5'-triphosphates of 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil, 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine, 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methylcytosine, 9-[(2-hydroxyethoxy)methyl]guanine, and 9-(1,3-dihydroxy-2-propoxymethyl)guanine had lower Ki values for Epstein-Barr virus DNA polymerase than has been reported elsewhere for host DNA polymerase. Inhibition of DNA elongation by these analogs ranged from moderate to strong, suggesting that preferential incorporation of these analogs into DNA by virus DNA polymerase may contribute to antiviral selectivity.

IT **79551-89-6**
RL: BIOL (Biological study)
(Epstein-Barr virus DNA polymerase interaction with)
RN 79551-89-6 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 95 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:178764 HCAPLUS
DOCUMENT NUMBER: 102:178764

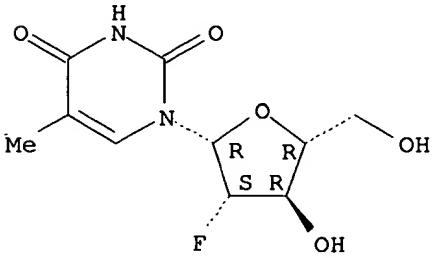
TITLE: Treatment of genital herpes simplex virus infections in guinea pigs
AUTHOR(S): Kern, Earl R.
CORPORATE SOURCE: Sch. Med., Univ. Utah, Salt Lake City, UT, 84132, USA
SOURCE: UCLA Symp. Mol. Cell. Biol., New Ser. (1984), 21(Herpesvirus), 617-36
CODEN: USMBD6; ISSN: 0735-9543
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intravaginal inoculation of guinea pigs with herpes simplex virus type 2 provides an excellent model for genital herpes in humans. The infection is characterized by local viral replication in the vaginal tract followed by the appearance of vesicular lesions on external genital skin. After recovery from the primary infection, spontaneous recurrent lesions appear on the external genitalia. Oral treatment with acyclovir [59277-89-3], 2'-deoxy-2'-fluoro-5-iodoarabinosylcytosin [69123-90-6], 2'-fluoro-5-iodoarabinosyluracil [69123-98-4], 2'-fluoro-5-methylarabinosyluracil [**69256-17-3**], 9-(1,3-dihydroxy-2'-propoxymethyl)guanine [82410-32-0], and i.m. treatment with recombinant human interferon-.alpha.A all reduced the severity of the primary infection. All compds. administered during recurrent disease also reduced the frequency of recurrent episodes, however, the frequency of recurrences returned to the level of controls when therapy was terminated.

IT **69256-17-3**
RL: BIOL (Biological study)
(genital herpes simplex virus infection treatment with)

RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 96 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:146012 HCAPLUS
DOCUMENT NUMBER: 102:146012
TITLE: Drug resistant and hypersensitive herpes simplex virus mutants: isolation and application to dissection of the pol locus
AUTHOR(S): Coen, Donald M.; Chiou, Henry C.; Fleming, H. Edward, Jr.; Leslie, Laurel K.; Retondo, Margaret J.
CORPORATE SOURCE: Dep. Pharmacol., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: UCLA Symp. Mol. Cell. Biol., New Ser. (1984), 21(Herpesvirus), 373-85
CODEN: USMBD6; ISSN: 0735-9543
DOCUMENT TYPE: Journal
LANGUAGE: English

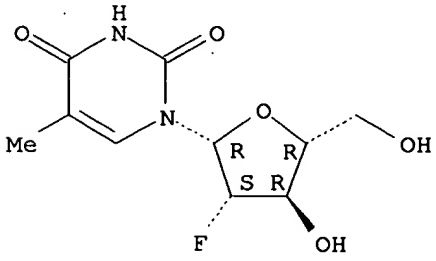
AB Herpes simplex virus mutants resistant to antiviral drugs and aphidicolin are readily isolated in a single-step selection procedure. However, it

was found that mutants resistant to one drug are often not substantially cross-resistant to others suggesting possible solns. to potential clin. resistance. Repeated plaque purifn. has proven essential for such analyses. Previous studies have identified PAA-, ACG-, and araA-resistance mutations in the DNA polymerase (pol) locus. Mutations conferring hypersensitivity to araA, PAA, FMAU, FIAU, BVdU, 2'NDG, and aphidicolin (Aph) were identified and several of these were mapped to the pol locus. The existence of either type of mutation in the pol locus implies that polymerase is a target for the drugs or otherwise mediates drug-sensitivity. Addnl., cross-resistance patterns of the mutants suggest that polymerases capable of discriminating against one **nucleoside** analog are incapable of discriminating against closely related compds. Mutations conferring altered sensitivity to the same drug map at different locations in the pol locus. Anal. of these mutations should aid in the functional dissection of the polymerase.

IT **69256-17-3**
RL: BIOL (Biological study)
(resistance to, of herpes simplex virus, DNA polymerase gene in relation to)

RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 97 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:113894 HCAPLUS
DOCUMENT NUMBER: 102:113894
TITLE: Nucleosides
INVENTOR(S): Hertel, Larry Wayne
PATENT ASSIGNEE(S): Lilly, Eli, and Co. , USA
SOURCE: Brit. UK Pat. Appl., 17 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2136425	A1	19840919	GB 1984-5805	19840306
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US 4526988	A	19850702	US 1983-473883	19830310
DK 8401144	A	19840911	DK 1984-1144	19840228
DK 162529	B	19911111		
DK 162529	C	19920330		
RO 89963	B3	19860930	RO 1984-113763	19840229
ZA 8401605	A	19851030	ZA 1984-1605	19840302
CA 1218647	A1	19870303	CA 1984-448698	19840302
IL 71143	A1	19880731	IL 1984-71143	19840304
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HU 193893	B	19871228			
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PRIORITY APPLN. INFO.:

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IL 1984-71143	19840304
EP 1984-301463	19840306
GB 1984-5805	19840306

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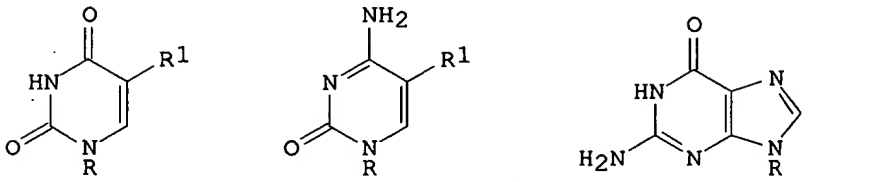

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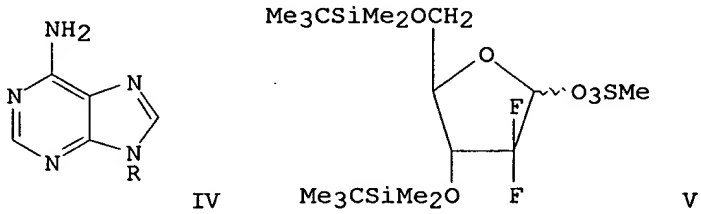


IV V

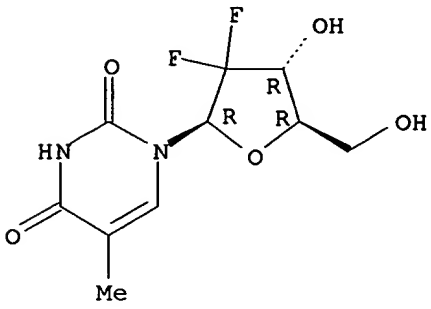
AB Difluoro nucleosides I-IV [R = 2-deoxy-2,2-difluoro-.alpha.(.beta.)-D-pentofuranosyl; R1 = H, Me, halogen, CH:CHR2; R2 = Cl, Br, iodo] were prepd. Thus, 4-formyl-2,2-dimethyldioxolane, prepd. from D-glyceraldehyde, was condensed with BrCF2CO2Et to give a 3:1 mixt. of Et (3R)- and (3S)-2,2-difluoro-3-hydroxy-3-(2,2-dimethyldioxolan-4-yl)propionate. The 3R-isomer was hydrolyzed to give the ribonolactone, which was tert-butyldimethylsilylated, reduced with (Me2CHCH2)2AlH, and mesylated to give ribose deriv. V. V was condensed with 5-methyl-2,4-bis(trimethylsiloxy)pyrimidine to give the silylated **nucleoside** which was desilylated with HBr to give I [R = 2-deoxy-2,2-difluoro-.alpha.(.beta.)-ribofuranosyl, R1 = Me; VI]. .beta.-VI at 0.31 .mu.g/mL inhibited the growth of herpes simplex virus, type 1 by 50% compared with 7.6 and 1.74 .mu.g/mL for Ara-A and Acyclovir,

resp.

IT **95058-80-3P 95058-84-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and virucidal activity of)

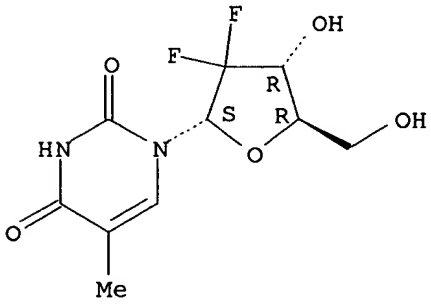
RN 95058-80-3 HCAPLUS
CN Thymidine, 2',2'-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 95058-84-7 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2,2-difluoro-.alpha.-D-erythro-pentofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 98 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:109059 HCAPLUS
DOCUMENT NUMBER: 102:109059
TITLE: Quantitative autoradiographic mapping of focal herpes simplex virus encephalitis using a radiolabeled antiviral drug
INVENTOR(S): Price, Richard
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4489052	A	19841218	US 1982-418156	19820915

AB A diagnostic, noninvasive test for herpes simplex virus (HSV) type 1 encephalitis is described that is based on the selective uptake by infected cells of radiolabeled antiviral drug, consisting of 5-substituted
1-(2'-deoxy-2'-substituted .beta.-D-arabinofuranosyl)pyrimidine

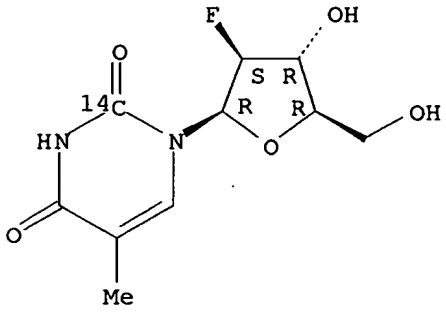
nucleoside, and external scanning by positron emission tomog. or gamma scanning. For example, female CD rats infected with HSV-1 were administered [2-14C]FMAU (2'-fluoro-5-methyl-1-.beta.-D-arabinofuranosyl[2-14C]uracil) (47.5 .mu.Ci/mg). 14C activity in infected regions exceeded background in all HSV-1 infected rats. FMAU showed rapid blood clearance and was excreted mainly in unchanged form. The organ distribution of [2-14C]FMAU in HSV-1 infected rats is presented. Suitable labels for use in positron emission tomog. or gamma scanning are discussed.

IT **83374-60-1**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metab. of, in herpes simplex virus type 1 encephalitis, positron tomog. or scintigraphy in relation to)

RN 83374-60-1 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione-2-14C, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 99 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1985:105771 HCAPLUS

DOCUMENT NUMBER: 102:105771

TITLE: Sensitivity of arabinosyladenine-resistant mutants of herpes simplex virus to other antiviral drugs and mapping of drug hypersensitivity mutations to the DNA polymerase locus

AUTHOR(S): Coen, Donald M.; Fleming, H. Edward, Jr.; Leslie, Laurel K.; Retondo, Margaret J.

CORPORATE SOURCE: Dep. Pharmacol., Harvard Med. Sch., Boston, MA, 02115, USA

SOURCE: J. Virol. (1985), 53(2), 477-88
CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE: Journal

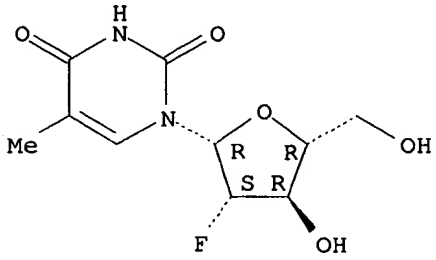
LANGUAGE: English

AB Seven herpes simplex virus mutants which have been previously shown to be resistant to arabinosyladenine [5536-17-4] were examd. for their sensitivities to 4 types of antiviral drugs. These drugs were a pyrophosphate analog, 4 **nucleoside** analogs altered in their sugar moieties, 2 **nucleoside** analogs altered in their base moieties, and 1 altered in both. The 7 mutants exhibited 5 distinct phenotypes based on their sensitivities to the drugs relative to wild-type strain KOS. All mutants exhibited resistance to acyclovir [59277-89-3] and arabinosylthymine [605-23-2], as well as marginal resistance to iododeoxyuridine [54-42-2], whereas all but one exhibited resistance to phosphonoformic acid [4428-95-9]. The mutants exhibited either sensitivity or hypersensitivity to the other drugs tested, 2'-nor-deoxyguanosine [82410-32-0], 5-methyl-2'-fluoroarauracil [**69256-17-3**], 5-iodo-2'-fluoroarauracil [69123-98-4], and bromovinyldeoxyuridine [82768-44-3], some of which differed only slightly

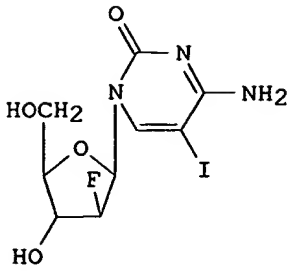
from drugs to which the mutants were resistant. These results suggest ways to detect and treat arabinosyladenine-resistant isolates in the clinic. Antiviral hypersensitivity was a common phenotype. Mutations conferring hypersensitivity to 2'-nor-deoxyguanosine in mutant PAAr5 and to bromovinyldeoxyridine in mutant tsD9 were mapped to nonoverlapping regions of 1.1 and 0.8 kilobase pairs, resp., within the herpes simplex virus DNA polymerase [9012-90-2] locus. Thus, viral DNA polymerase mediates sensitivity to these 2 drugs. However, reports of mutations in the DNA polymerase locus conferring resistance to these 2 drugs could not be confirmed. All of the mutants exhibited altered sensitivity to .gtoreq.2 types of drugs, suggesting that single mutations affect recognition of the base, sugar, and triphosphate moieties of **nucleoside** triphosphates by viral polymerase.

IT **69256-17-3**
RL: BIOL (Biological study)
(herpes simplex virus hypersensitivity to, arabinosyladenine resistance
and DNA polymerase gene in relation to)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione,
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-
5-methyl- (9CI) (CA INDEX NAME)

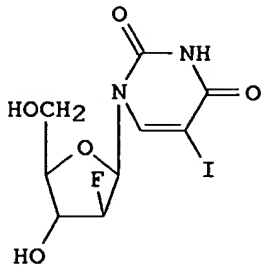
Absolute stereochemistry.



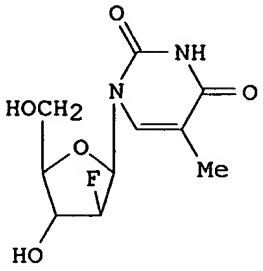
L11 ANSWER 100 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:39537 HCAPLUS
DOCUMENT NUMBER: 102:39537
TITLE: Cell-specific antiviral activity of 1-(2-fluoro-2-deoxy-.beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) against Marek's disease herpesvirus and turkey herpesvirus
AUTHOR(S): Schat, Karel A.; Schinazi, Raymond F.; Calnek, Bruce W.
CORPORATE SOURCE: New York State Coll. Vet. Med., Cornell Univ., Ithaca,
NY, 14853, USA
SOURCE: Antiviral Res. (1984), 4(5), 259-70
CODEN: ARSRDR; ISSN: 0166-3542
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II



III

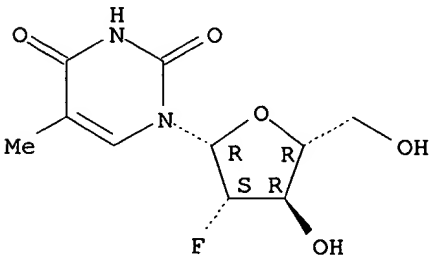
AB Three new fluoroarabinosylpyrimidine nucleosides [1-(2-fluoro-2-deoxy-.beta.-D-arabinofuranosyl-5-iodocytosine (FIAC)(I) [69123-90-6], 1-(2-fluoro-2-deoxy-.beta.-D-arabinofuranosyl)-5-iodouracil (FIAU)(II) [69123-98-4], and 1-(2-fluoro-2-deoxy-.beta.-D-arabinofuranosyl)-5-methyluracil (FMAU)(III) [**69256-17-3**]] were tested for in vitro activity against oncogenic and nononcogenic strains of Marek's disease virus (MDV) and herpesvirus of turkeys (HVT). Marek's disease is a herpesvirus-induced lymphoma in chickens. Nononcogenic strains of MDV and HVT can protect against this disease. All viruses were inhibited by 1 .mu.M of these drugs in chick kidney cell (CKC) cultures, but only FMAU and FIAU were active in chicken embryo fibroblast (CEF) and spleen cell cultures. It was detd. that whereas CKC produced the enzyme 2'-deoxycytidine-deaminase [37259-56-6] which is needed to deaminate FIAC to FIAU, CEF were devoid of this enzyme activity. In addn., the deaminase inhibitor 3,4,5,6-tetrahydrouridine prevented the antiviral activity of FIAC and CKC. FMAU was not active against two Marek's disease-derived lymphoblastoid tumor cell lines.

IT **69256-17-3**
RL: BIOL (Biological study)
(Marek's disease and herpes virus infection prevention with)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 101 OF 115 HCAPLUS COPYRIGHT 2000 ACS

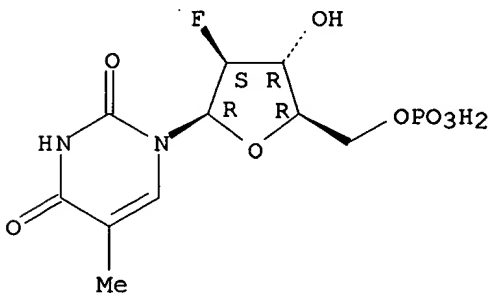
ACCESSION NUMBER: 1985:39529 HCAPLUS
DOCUMENT NUMBER: 102:39529
TITLE: Kinetics of the interaction of monophosphates of the antiviral nucleosides 2'-fluoro-1-.beta.-D-arabinofuranosylpyrimidine and (E)-5-(2-bromovinyl)-2'-deoxyuridine with thymidylate kinases from Vero cells and herpes simplex virus types 1 and 2
AUTHOR(S): Chen, Ming S.; Amico, Leonard A.; Speelman, Dan J.
CORPORATE SOURCE: Pharm. Res. and Dev. Div., Bristol-Myers, Syracuse, NY, 13221-4755, USA
SOURCE: Antimicrob. Agents Chemother. (1984), 26(5), 778-80
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The affinities of the monophosphates of 2'-fluoro-5-iodo-1-.beta.-D-arabinofuranosyluracil and its 5-Me analog for cellular thymidylate kinase [9014-43-1] were two or more orders of magnitude greater than for the thymidine-thymidylate kinase [9002-06-6] from herpes simplex virus types 1 and 2. In contrast, the monophosphate of (E)-5-(2-bromovinyl)-2'-deoxyuridine [80860-82-8] was found to have a higher affinity for the viral enzymes than for the cellular enzyme.

IT **94344-82-8**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(thymidylate kinase of herpes simplex virus response to)

RN 94344-82-8 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-5-O-phosphono-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L11 ANSWER 102 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1984:566417 HCAPLUS
DOCUMENT NUMBER: 101:166417
TITLE: The inhibition of ultraviolet radiation-induced DNA repair in human diploid fibroblasts by arabinofuranosyl nucleosides
AUTHOR(S): Snyder, Ronald D.; Van Houten, Bennett; Regan, James D.
CORPORATE SOURCE: Stauffer Chem. Co., Farmington, CT, 06032, USA
SOURCE: Chem.-Biol. Interact. (1984), 50(1), 1-14
CODEN: CBINA8; ISSN: 0009-2797
DOCUMENT TYPE: Journal
LANGUAGE: English

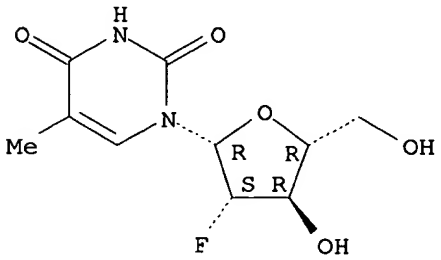
AB The antiviral compds. 9-.beta.-D-arabinofuranosyladenine (ara-A), 9-.beta.-D-arabinofuranosyl-2-fluoroadenine (FAA), 9-.beta.-D-

arabinofuranosylhypoxanthine (ara-Hx), 9-.beta.-D-arabinofuranosylguanine (ara-G), 1-.beta.-D-arabinofuranosylthymine (ara-T), 1-.beta.-D-arabinofuranosyl-2'-fluorocytosine (FAC), 1-.beta.-D-arabinofuranosyl-2'-fluoro-5-iodocytosine (FIAC), and 1-.beta.-D-arabinofuranosyl-2'-fluoro-5-methyluracil (FMAU) were compared to 1-.beta.-D-arabinofuranosyl cytosine (ara-C) in their ability to inhibit UV light-induced DNA repair in log phase and confluent human diploid fibroblasts. Inhibition of the polymn. or ligation steps of DNA excision repair manifests itself in the form of DNA single-strand breaks which may be quantitated through velocity sedimentation anal. in alk. sucrose gradients. In UV-irradiated quiescent, confluent human fibroblast cultures, treatment with any of the aranucleosides leads to accumulation of single-strand breaks but the ED for this inhibition varies greatly. The order of their effectiveness in confluent cultures was ara-C and its derivs. >ara-A, FAA, ara-G, Ara-HX > ara-T. In rapidly cycling cells, on the other hand, sensitivity to repair inhibition was exhibited only in response to ara-C and FAC. If 2 mM hydroxyurea (HU) was administered with ara-A, FAA, or FMAU, however, DNA strand breaks were seen. HU also increased the efficiencies of ara-C and FAC. No strand breaks were obsd. in UV-irradiated log-phase cells treated with FIAC, ara-Hx, ara-G, or ara-T even in the presence of HU. The efficiencies of inhibition of unscheduled DNA synthesis (UDS) and semiconservative DNA synthesis by the aranucleosides is consistent with their relative efficiencies at producing strand breaks. The ability of the aranucleosides to inhibit DNA is discussed with respect to their hypothesized effects on DNA metabolic processes in eukaryotic cells.

IT **69256-17-3**
RL: BIOL (Biological study)
(DNA repair in human fibroblasts induction by UV radiation inhibition by)

RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 103 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER:	1984:64869 HCAPLUS
DOCUMENT NUMBER:	100:64869
TITLE:	Effects of certain **nucleoside** analogs on human cytomegalovirus replication in vitro
AUTHOR(S):	Mar, Engchun; Patel, Pravin C.; Cheng, Yungchi; Fox, Jack J.; Watanabe, Kyoichi A.; Huang, Engshang
CORPORATE SOURCE:	Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE:	J. Gen. Virol. (1984), 65(1), 47-53 CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE:	Journal
LANGUAGE:	English

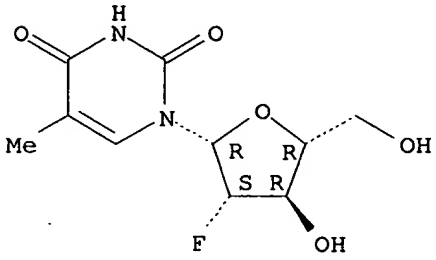
AB Four **nucleoside** analogs, 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil (I), -5-iodouracil (II),

-5-methylcytosine (III) and -5-iodocytosine (IV), were studied for their effect on human cytomegalovirus (HCMV) replication in vitro. I, II, III, and IV showed antiviral activities for 4 strains of HCMV (Major, Clegg, D550 and Towne) in a plaque redn. assay, with ED50s in the range of 0.1-0.65 .mu.M. At 1 .mu.M I or IV, the synthesis of 5 virus-specific late polypeptides was entirely blocked. Quantification of Towne viral DNA synthesis, using complementary RNA-DNA hybridization with a Towne-specific cRNA probe, demonstrated a complete inhibition of HCMV DNA replication at 1 .mu.M I or IV. After the removal of the inhibitors, however, viral DNA synthesis resumed, and infectious virus reappeared, indicating that the inhibition of HCMV replication by these **nucleoside** analogs was of a virostatic reversible type.

IT **69256-17-3**
RL: BIOL (Biological study)
(human cytomegalovirus replication inhibition by)

RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 104 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1984:48296 HCAPLUS
DOCUMENT NUMBER: 100:48296
TITLE: Alterations in the recognition of **nucleoside** analogs as substrates by the deoxythymidine kinase of a 5-methoxymethyldeoxyuridine-resistant mutant of herpes simplex virus type 1
AUTHOR(S): Veerisetty, V.; Veerisetty, Indira K.; Gentry, Glenn A.
CORPORATE SOURCE: Med. Cent., Univ. Mississippi, Jackson, MS, 39216, USA
SOURCE: J. Gen. Virol. (1983), 64(12), 2767-70
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inhibition consts. (Kis) were used as an est. of the ability of various **nucleoside** analogs to be recognized as substrates by the deoxythymidine kinases (dTKs) of a 5-methoxymethyldeoxyuridine-resistant (MMdUr) mutant of herpes simplex virus type 1 (HSV-1) and its parent wild-type (wt). The Kis for the 5-position analogs MMdU, [E]-5-(2-bromovinyl)deoxyuridine, bromodeoxyuridine, and iododeoxyuridine were increased approx. 3-5-fold, suggesting that they were poorer substrates for the MMdUr dTK than for the wt dTK. With the 2' analogs arabinosylthymine and 2'-fluoro-5-methylarabinosyluracil, however, the Kis were increased to a much greater extent, 80- and 240-fold, resp. These findings suggest that the resistance of the mutant MMdUr to these analogs may be due to a mutation(s) in the viral dTK that directly affects binding at the 2' recognition site and indirectly at the 5, while still allowing

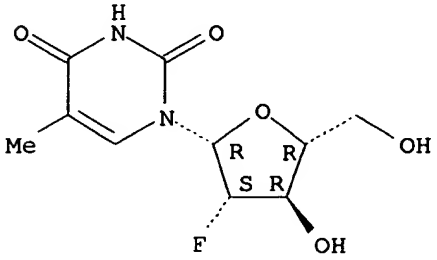
substantial activity with the natural substrate deoxythymidine.

IT **69256-17-3**
RL: BIOL (Biological study)
(as substrate, deoxythymidine kinase of methoxymethyldeoxyuridine-resistant mutant of herpes simplex virus recognition of)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 105 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1983:609169 HCAPLUS

DOCUMENT NUMBER: 99:209169

TITLE: Prospects for the use of radiolabeled antiviral drugs in the diagnosis of herpes simplex encephalitis

AUTHOR(S): Price, Richard W.; Saito, Yutaka; Fox, Jack J.

CORPORATE SOURCE: Cotzias Lab. Neuro-Oncol., Meml. Sloan-Kettering Cancer Cent., New York, NY, 10021, USA

SOURCE: Biochem. Pharmacol. (1983), 32(17), 2455-61
CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

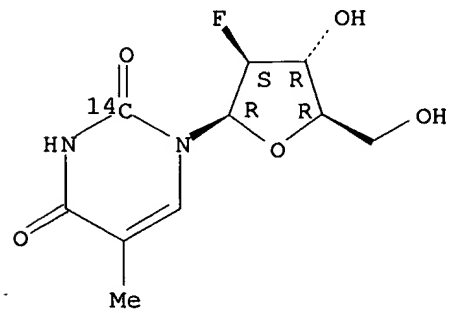
AB The title method is described and discussed. As an example, rats were intraocularly inoculated with herpes simplex encephalitis type 1 and i.v. injected with carbon-14-labeled 2'-fluoro-5-methyl-1-.beta.-D-arabinosyluracil (I); brains were then removed and in-vivo uptake of I was detected by autoradiog. with computer reconstruction as described by Y. Saito et al. (1982). Although improvements are still needed, this method is potentially useful for early specific diagnosis of herpes simplex in humans by various in-vivo scanning methods.

IT **83374-60-1**
RL: ANST (Analytical study)
(for diagnosis of herpes simplex encephalitis)

RN 83374-60-1 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione-2-14C, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

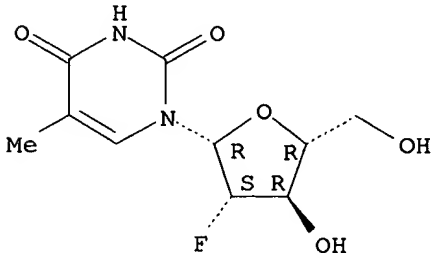


L11 ANSWER 106 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1983:605677 HCAPLUS
DOCUMENT NUMBER: 99:205677
TITLE: Efficacy and selectivity of some **nucleoside** analogs as antihuman cytomegalovirus agents
AUTHOR(S): Colacino, Joseph M.; Lopez, Carlos
CORPORATE SOURCE: Lab. Herpesvirus Infect., Sloan-Kettering Inst. Cancer Res., New York, NY, 10021, USA
SOURCE: Antimicrob. Agents Chemother. (1983), 24(4), 505-8
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1-(2'-Deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) [69123-90-6], 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluridine (FMAU) [**69256-17-3**], 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-iodouridine (FIAU) [69123-98-4], and 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-ethyluridine (FEAU) [83546-42-3] were evaluated for antiviral activities against human cytomegalovirus (HCMV) and compared with 9-[(2-hydroxyethoxy)methyl]guanine (acylovir) [59277-89-3] and E-5-(2'-bromovinyl)-2'-deoxyuridine (BVDU) [69304-47-8]. The relative anti-HCMV potencies of these compds., as detd. by calcg. the dose of drug which inhibited 50% plaque formation, were in order of decreasing potency:
FIAC > FIAU > FMAU > acyclovir > FEAU > BVDU. The antiviral activity of FIAC occurred at levels much lower than those that caused cytotoxic or cytostatic effects in uninfected fibroblasts. Neither thymidine nor deoxycytidine reversed the anti-HCMV activity of FIAC, indicating that this drug was not acting as an analog of the natural nucleosides. FIAC was not phosphorylated by cytosols of HCMV-infected cells to a greater extent that by those of uninfected cells, indicating that, unlike the antiviral activity against herpes simplex virus type 1, the selectivity of this drug is probably not based on a virus-specified pyrimidine kinase.

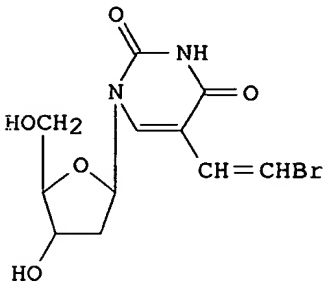
IT **69256-17-3**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(virucidal activity of, against humans cytomegalovirus)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

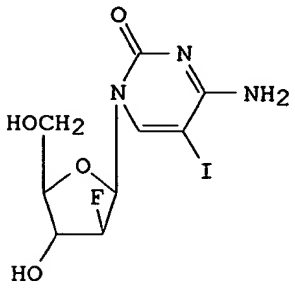


L11 ANSWER 107 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1983:515621 HCAPLUS
DOCUMENT NUMBER: 99:115621
TITLE: Epstein-Barr virus: inhibition of replication by three new drugs
AUTHOR(S): Lin, Jung Chung; Smith, M. Carolyn; Cheng, Yung Chi; Pagano, Joseph S.

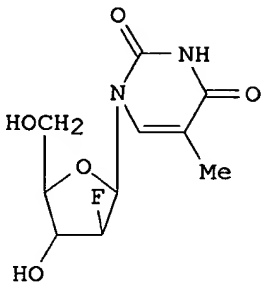
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: Science (Washington, D. C., 1883-) (1983), 221(4610), 578-9
CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II



III

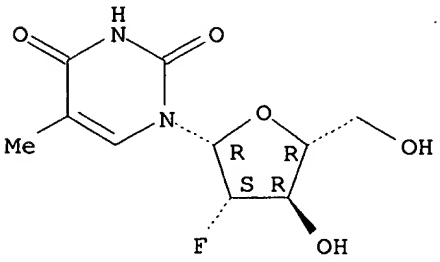
AB Acyclovir [59277-89-3], the first clin. useful drug effective against replication of Epstein-Barr virus (EBV) was without effect against latent or persistent EBV infection. Three **nucleoside** analogs, E-5-(2-bromovinyl)-2'-deoxyuridine (I) [69304-47-8], 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine (II) [69123-90-6] and 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil (III) [**69256-17-3**] were potent inhibitors of EBV replication in vitro. Moreover, in contrast to the reversibility of viral inhibition by acyclovir, these 3 drugs have prolonged effects in suppressing viral replication even after the drugs are removed from persistently infected cell cultures.

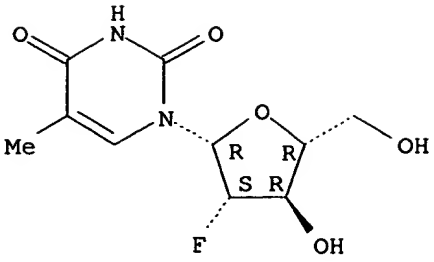
IT **69256-17-3**
RL: BIOL (Biological study)
(Epstein-Barr virus replication inhibition by)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

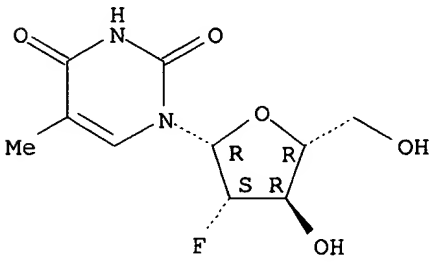
Absolute stereochemistry.





L11 ANSWER 108 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1983:154910 HCAPLUS
DOCUMENT NUMBER: 98:154910
TITLE: Structure-activity relationship of ligands of the pyrimidine **nucleoside** phosphorylases
AUTHOR(S): Niedzwicki, John G.; El Kouni, Mahmoud H.; Chu, Shih Hsi; Cha, Sungman
CORPORATE SOURCE: Div. Biol. Med., Brown Univ., Providence, RI, 02912, USA
SOURCE: Biochem. Pharmacol. (1983), 32(3), 399-415
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Eighty-seven pyrimidine base and **nucleoside** analogs were evaluated as inhibitors of uridine phosphorylase (UrdPase) [289-95-2] and thymidine phosphorylase (dThdPase) [9030-23-3]. These findings, together with an extensive literature review, have allowed construction of structure-activity relationships for the binding of ligands to UrdPase and dThdPase and provide a basis for the rational design of new inhibitors of these enzymes. Addnl., 2,6-pyridinediol [626-06-2] and 6-benzyl-2-thiouracil [6336-50-1] were identified as being potent inhibitors of UrdPase and dThdPase, resp.
IT **69256-17-3**
RL: BIOL (Biological study)
(pyrimidine **nucleoside** phosphorylase inhibition by, structure in relation to)
RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

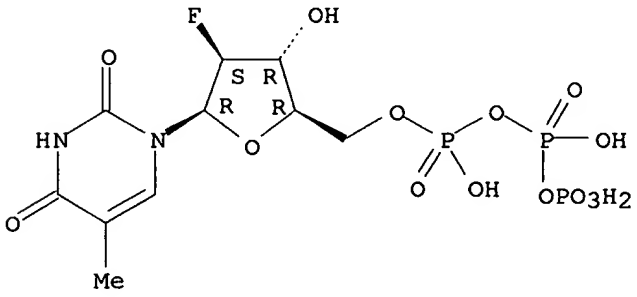
Absolute stereochemistry.



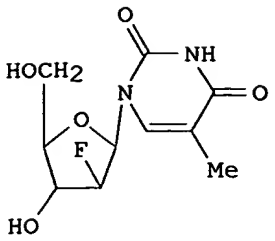
L11 ANSWER 109 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1982:484821 HCAPLUS
DOCUMENT NUMBER: 97:84821
TITLE: Differential effect of **nucleoside** analog triphosphates on ribonucleotide reductases from uninfected and herpes simplex virus-infected HeLa

cells
AUTHOR(S): Nakayama, Koji; Ruth, Jerry L.; Cheng, Yung C.
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: J. Virol. (1982), 43(1), 325-7
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of the triphosphates of 8 pyrimidine **nucleoside** analogs (5-substituted, 2'-fluoroara-, and acyclonucleosides) and acycloguanosine were examd. on ribonucleotide reductase [9040-57-7] prepd. from uninfected and herpes simplex virus types 1- and 2-infected HeLa cells. Of the analogs tested, E-5-propenyl- [79551-91-0] and E-5-(2-bromovinyl)-dUTP [77222-61-8] were more potent inhibitors of the enzyme from virus-infected cells than was dTTP [365-08-2]. In uninfected cells acyclo-TTP [82617-27-4] was the most effective inhibitor. The results are discussed in relation to the antiviral activities of the analogs.
IT **79551-89-6**
RL: BIOL (Biological study)
(ribonucleotide reductase from uninfected and herpes simplex virus-infected HeLa cells response to)
RN 79551-89-6 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 110 OF 115 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1982:466080 HCAPLUS
DOCUMENT NUMBER: 97:66080
TITLE: Activity of 2-fluoro-5-methylarabinofuranosyluracil against mouse leukemias sensitive to and resistant to 1-.beta.-D-arabinofuranosylcytosine
AUTHOR(S): Burchenal, J. H.; Chou, T. C.; Lokys, L.; Smith, R. S.; Watanabe, K. A.; Su, T. L.; Fox, J. J.
CORPORATE SOURCE: Mem. Sloan-Kettering Cancer Cent., New York, NY, 10021, USA
SOURCE: Cancer Res. (1982), 42(7), 2598-600
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

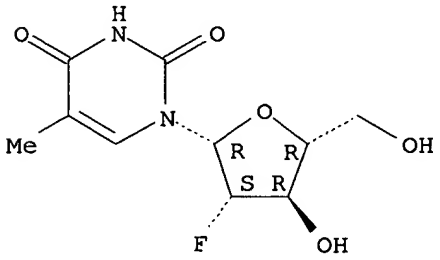
AB A new pyrimidine **nucleoside**, 2'-fluoro-5-methyl-1-.beta.-D-arabinofuranosyluracil (I) [**69256-17-3**] was active against mouse and human leukemic cells in culture and against mouse leukemias L1210, P388, and P815 in vivo. In contrast to other 1-.beta.-D-arabinofuranosylcytosine (ara-C) [147-94-4] derivs., I, when given either i.p. or orally, was highly active against lines of leukemias P815 and L1210 made resistant to ara-C. Against P815/ara-C and L1210/ara-C, it is more effective than is 5- azacytidine, a drug which has shown definite effectiveness in patients with acute leukemia resistant to ara-C. Thus, I may be useful in treatment of ara-C resistant leukemias.

IT **69256-17-3**
RL: BIOL (Biological study)
(leukemia inhibition by, ara-C resistance in relation to)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 111 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1982:85896 HCAPLUS

DOCUMENT NUMBER: 96:85896

TITLE: 2'-Fluoroarabinosyl pyrimidine nucleosides: chemistry, antiviral, and potential anticancer activities

AUTHOR(S): Fox, J. J.; Lopez, C.; Watanabe, K. A.

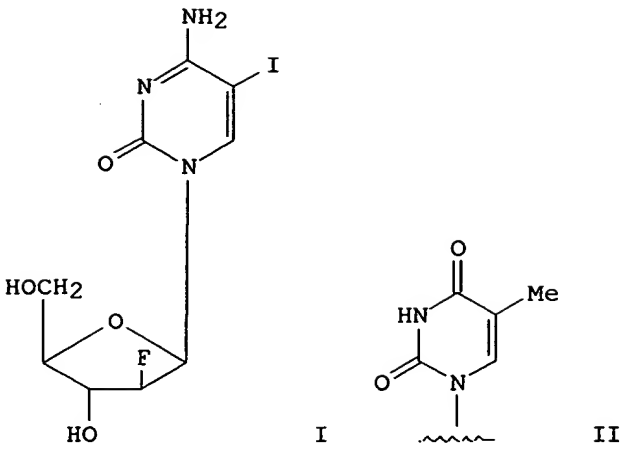
CORPORATE SOURCE: Mem. Sloan-Kettering Cancer Cent., Sloan-Kettering Inst., New York, NY, USA

SOURCE: Med. Chem. Adv., Proc. Int. Symp., 7th (1981), Meeting Date 1980, 27-40. Editor(s): De las Heras, Federico G.; Vega, Salvador. Pergamon: Oxford, Engl. CODEN: 46NHAC

DOCUMENT TYPE: Conference

LANGUAGE: English

GI



I II

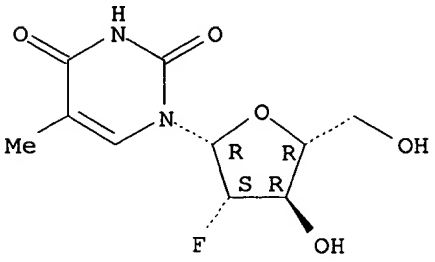
AB A series of 2'-fluoro-5-substituted-arabinofuranosyl-cytosines and -uracils were prepd. Two of these I and II, were found to be very potent and highly selective against herpes simplex virus (HSV) types 1 and 2 at very low drug levels. Cytotoxicity to uninfected Vero or human fibroblast cell proliferation was minimal. The selectivity of I against HSV vs. its low cytotoxicity against Vero cells is due, at least in part, to a virus-specificed thymidine kinase. Structure-activity studies demonstrate that the 2'-fluoro substituent in the up (arabino) configuration is essential for this potent antiviral activity. Substitution of the 2'-fluoro group by chloro or bromo reduces the antiviral potency. I is also active in a plaque redn. assay against herpes zoster virus at concn. of 0.01 .mu.M and against cytomegalovirus plaque formation at 0.1 .mu.M. In vivo studies in mice inoculated with 20 LD50 of HSV-1 show that I and II are effective, the latter giving 60% cures at dose levels as low as 1 mg/kg/day x5. The selective cytotoxicity of I against human tumor cell lines but not against normal human cells is discussed.

IT **69256-17-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and virucidal activity of)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 112 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1981:614866 HCAPLUS

DOCUMENT NUMBER: 95:214866

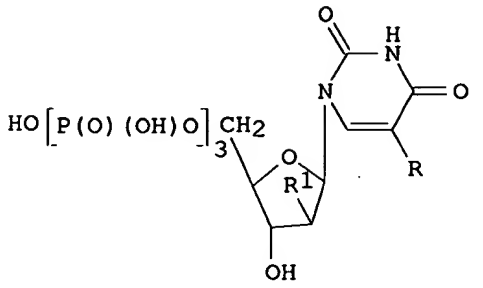
TITLE: **Nucleoside** analogs with clinical potential in antivirus chemotherapy. The effect of several thymidine and 2'-deoxycytidine analog 5'-triphosphates

on purified human (.alpha., .beta.) and herpes simplex virus (types 1, 2) DNA polymerases

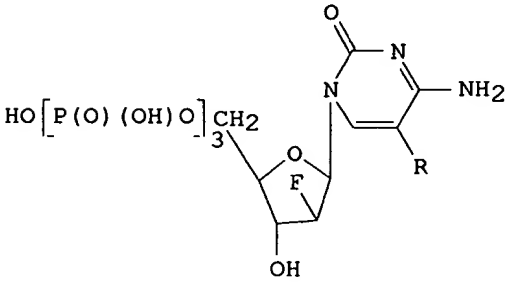
AUTHOR(S): Ruth, Jerry L.; Cheng, Yung Chi
CORPORATE SOURCE: Cancer Res. Cent., Univ. North Carolina, Chapel Hill, NC, 27514, USA

SOURCE: Mol. Pharmacol. (1981), 20(2), 415-22
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



I



II

AB To aid in establishing the mechanisms of antiherpes virus action and the basis for selectivities of 7 **nucleoside** analogs, I (R = Me, Pr, CH:CHMe, or CH:CHBr, R1 = H or OH) and II (R = Me or I) were prepd. for testing with DNA polymerase [9012-90-2]; a general method for the direct chem. synthesis of **nucleoside** triphosphate from **nucleoside** is described. The effects of the analog triphosphates were evaluated on the following 4 isolated DNA polymerases: virus-induced DNA polymerases from herpes simplex virus Type 1 (HSV-1) and Type 2 (HSV-2) infections, and human DNA polymerases .alpha. and .beta., using conditions optimal for each. Competitive inhibition results indicate that all 7 analog triphosphates are good inhibitors of normal substrate utilization by DNA polymerase regardless of enzyme source, have much higher apparent affinities (20- to 600-fold lower Ki) for HSV polymerases than for human polymerases, and are equally inhibitory to both HSV-1 and HSV-2 DNA polymerases. The analogs varied considerably in support of DNA synthesis in the absence of normally competing substrate, again with little difference between polymerases. The relative ability to support DNA synthesis was generally E-5-propenyl-dUTP [79551-91-0] .simeq. dTTP > E-5-(2-bromovinyl-dUTP) [77222-61-8] > 5-propyl-dUTP [64374-76-1] .mchgt. 2'-fluoro-arabinonucleoside triphosphates .mchgt. E-5-(2-bromovinyl)-araUTP [79551-90-9]. Incubation of analog triphosphates and polymerase with activated DNA suggests that, with E-5-(2-bromovinyl)-araUTP as the exception, the analogs have little effect on the subsequent ability of product DNA to serve as primer template. E-5-Propenyl-dUTP exhibited behavior the most similar to dTTP throughout these studies. Some general structure-activity relationships are

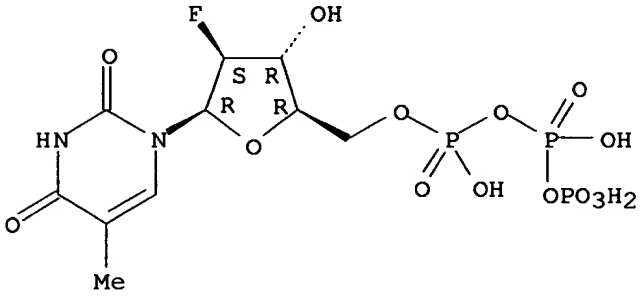
discussed.

IT **79551-89-6**
RL: BIOL (Biological study)
(DNA polymerase inhibition by, antiviral activity in relation to)

RN 79551-89-6 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 113 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1981:580671 HCAPLUS

DOCUMENT NUMBER: 95:180671

TITLE: Differential activity of potential antiviral **nucleoside** analogs on herpes simplex virus-induced and human cellular thymidine kinases

AUTHOR(S): Cheng, Y. C.; Dutschman, G.; Fox, J. J.; Watanabe, K. A.; Machida, H.

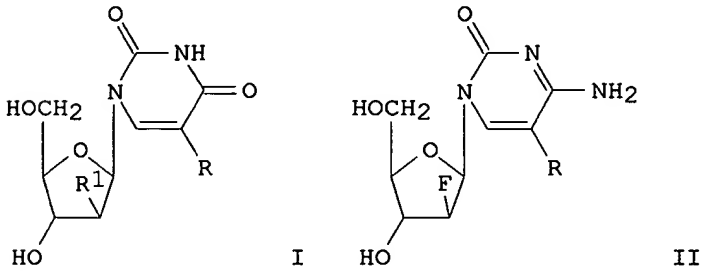
CORPORATE SOURCE: Cancer Cent., Univ. North Carolina, Chapel Hill, NC, 27514, USA

SOURCE: Antimicrob. Agents Chemother. (1981), 20(3), 420-3
CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I II

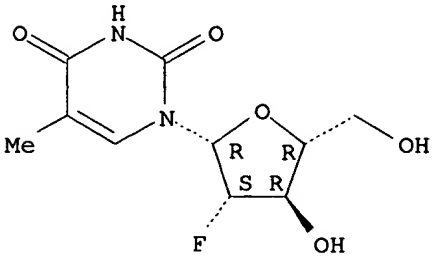
AB The rates of phosphorylation of the potential antiviral **nucleoside** analogs I (R = I, Me, CH:CHBr; R1 = H, F, OH) and II (R = I, Me) by purified thymidine kinase [9002-06-6] from both human and herpes simplex virus sources were studied. Most of the analogs were phosphorylated by both human and viral kinases. The analogs were competitive inhibitors of thymidine phosphorylation by the kinases; on the assumption that inhibition consts. (Ki) reflect binding affinity, Ki values of the analogs were detd. In general, the analogs have a greater affinity for the viral kinases than for the human kinases. The amt. of the analogs phosphorylated to the monophosphate form, which is presumably necessary

for cytotoxic activity, was dependent on both the phosphorylation rates and binding affinities. All of the analogs act as preferential substrates for the viral kinases at low concns., which may be one of the main reasons for their selective antiviral action. The structure-activity relations of the analogs are discussed.

IT **69256-17-3**
RL: BIOL (Biological study)
(phosphorylation of, by thymidine kinase, structure and virucidal activity in relation to)

RN 69256-17-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

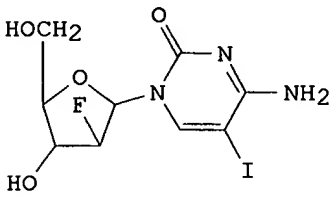
Absolute stereochemistry.



L11 ANSWER 114 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER:	1981:561687 HCAPLUS
DOCUMENT NUMBER:	95:161687
TITLE:	Pharmacological disposition and metabolic fate of 2'-fluoro-5-iodo-1-.beta.-D-arabinofuranosylcytosine in mice and rats
AUTHOR(S):	Chou, Ting-Chao; Feinberg, Aaron; Grant, Alan J.; Vidal, Pedro; Reichman, Uri; Watanabe, Kyoichi A.; Fox, Jack J.; Philips, Frederick S.
CORPORATE SOURCE:	Lab. Pharmacol., Sloan-Kettering Inst. Cancer Res., New York, NY, 10021, USA
SOURCE:	Cancer Res. (1981), 41(9, Pt. 1), 3336-42 CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE:	Journal
LANGUAGE:	English

GI



I

AB 2'-Fluoro-5-iodo-1-.beta.-D-arabinofuranosylcytosine-HCl (FIAC)(I) [69123-90-6] was synthesized and labeled with 14C in the 2 position for the study of pharmacol. disposition and metabolic fate. FIAC is deaminated by cytosine **nucleoside** deaminase [9025-06-3] at a rate comparable to that of 1-.beta.-D-arabinofuranosylcytosine. The deaminated product, 2'-fluoro-5-iodo-1-.beta.-D-arabinofuranosyluracil (FIAU) [69123-98-4] is, like FIAC, an active antiviral agent. After i.v.